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Genotyping CYP1A2, CYP2D6 and CYP2C19 Polymorphisms by HRM analysis for Personalized Medicine in Turkish Psychiatry Patients

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INTRODUCTION

Pharmacotherapy is the mainstay of treatment for the psychotic symptoms of mental conditions such as schizophrenia, bipolar disorder and major depression and can be used for the treatment of psychotic symptoms of demantias. The cytochrome P450 proteins are drug-metabolizing enzymes that involves in many catalytic reactions (1). Interindividual variability in drug response is a major problem in clinical practice. Interindividual variability in drug response is a major clinical problem (2). In this study we aimed to investigate the frequencies of CYP2D6, CYP1A2, CYP2C19 polymorphisms of schizophrenic and bipolar patients. That would be the first step to evaluate the therapeutic response may allow the treatment to be individualized for our patients.

METHODS

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 and*4), CYP1A2 (*1F) and CYP2C19 (*2 and *3) variants (3).

RESULTS

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

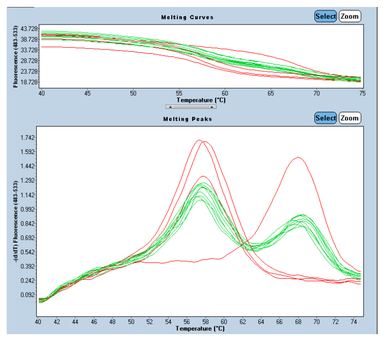


Figure 1. CYP1A *1F genotyping

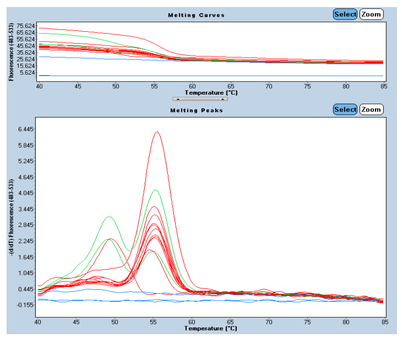


Figure 2. CYP2C19 *2 and *3 genotyping

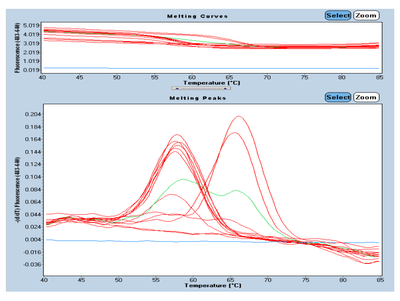


Figure 3. CYP2D6 *3 and *4 genotyping

Table 1. Genotype frequencies of study population

	Genotype	Number of Subjects (n= 101)	Observed Frequency % 95 CI
Psychosis			
CYP1A2 *1F	**1F/*1F*	26	48,1(35,2-61,1)
	**1A/*1F*	23	42,6 (29,6-57,4)
	**1A/*1A*	5	9,3 (1,9-16,7)
CYP2C19 *2 & *3	**1/*1*	44	81,5 (70,4-90,7)
	**1/*2*	8	14,8 (5,6-25,9)
	**1/*3*	0	0
	**2/*2*	2	3,7 (0-9,3)
	**3/*3*	0	0
	**2/*3*	0	0
CYP2D6 *3 & *4	**1/*1*	43	79,6 (68,5-88,9)
	**1/*3*	2	3,7 (0-9,3)
	**1/*4*	7	13,0 (5,6-22,2)
	**3/*3*	0	0
	**4/*4*	1	1,9 (0-5,6)
	**3/*4*	1	1,9 (0-5,6)
	Genotype	**Number of Subjects (n= 101)**	**Observed Frequency 95 % CI**
Bipolar Disease			
CYP1A2 *1F	**1F/*1F*	25	53,2 (38,3-66,0)
	**1A/*1F*	20	42,6 (29,8-57,4)
	**1A/*1A*	2	4,3 (0-10,6)
CYP2C19 *2 & *3	**1/*1*	37	78,7 (66,0-89,4)
	**1/*2*	9	19,1 (8,5-29,8)
	**1/*3*	0	0
	**2/*2*	1	2,1 (0-6,4)
	**3/*3*	0	0
	**2/*3*	0	0
CYP2D6 *3 & *4	**1/*1*	39	83,0 (72,3-93,6)
	**1/*3*	0	0
	**1/*4*	7	14,9 (6,4-25,5)
	**3/*3*	0	0
	**4/*4*	1	2,1 (0-8,5)
	**3/*4*	0	0

CONCLUSSION

Genetic polymorphism of human cytochrome P450 enzymes and receptors known in the treatment process, may be important to maintain the availability of the treatment (4). In the present study, we used high resolution melting as a simple, sensitive, reliable and accurate molecular assay to genotype the common CYP1A2, CYP2D6 and CYP2C19 variants in schizophrenia and bipolar disorder patients. The results showed that the CYP1A2 **1F* variant had a high frequency in our patients who require a substantial reduction in doses and careful management of drug association to avoid toxicity, thereby, providing the concept of individualized therapy (5). These pharmacogenetic tests can allow the clinicians to make accurate diagnosis, prescribe more efficient drug therapies and avoid harmful side effects. 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.

Acknowledgements

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