Searching Relevant Polymorphisms of CYP2B6 in HIV Infected Patients

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Review

The CYP2B6 belongs to the family of Cytochrome P450 enzymes that catalyze the metabolism of a wide variety of drugs, including the anti-retroviral EFV. The CYP2B6 gene, that has been mapped in the chromosome 19, is highly polymorphic and some SNP, namely 516G>T and 785A>G, are associated with decreased protein expression. These variants are related to phenotypes that are characterized as EFV poor metabolizers, and consequently to episodes of neurotoxicity.

Objective

Identification and characterization of the major CYP2B6 polymorphisms in 48 HIV patients receiving antiretroviral therapy with EFV.

Materials and Methods

SNP 516G>T

DNA Extraction

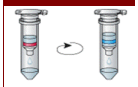
- PerfectPure DNA Blood Kit (5Prime

PCR-RFLP

Kit Illustra™ puReTaq Ready-To-Go PCR Beads

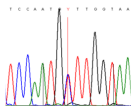
Enzimatic restriction with BsrI

PCR Products Purification



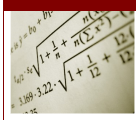
Kit NucleoSpin® Gel and PCR Clean-up

Sequencing Analysis



STAB-VIDA Laboratory

Statistical Analysis



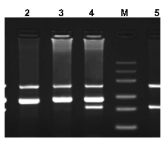
Hardy-Weinberg R package based on $\chi 2$ – test

SNP 785A>G

DNA Extraction

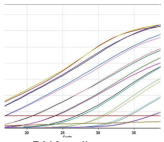
- PerfectPure DNA Blood Kit (5Prime

Nested PCR



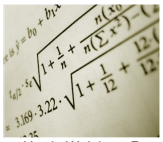
- PCR multiplex
- Alellic Speciific PCR

TaqMan® RT-PCR



DNA polimerase Thermus aquaticus

Statistical Analysis



Hardy-Weinberg R package based on $\chi 2$ – test

Population Characteristics

The sample was composed by 48 individuals infected with HIV-1 receiving ARV therapy with EFV. In terms of gender, 39 were male and 9 were female. Relatively to the race 39 were Caucasian and 9 African.

Results

All the samples were classified as having the 785AG genotype.

Of all the 48 patients, 21 had the 516GG genotype and 27 has the 516TT genotype, table 1.

None of the SNP were in Hardy-Weinberg equilibrium which may mean that the gene is evolving.

The genotype frequencies for the SNP 516G>T are the same among males and females (p-value > 0.05), table 2.

The comparison of frequencies for the 516G>T by races also doesn't show statistical significance, table 3.

Taking account to the results obtained, 27 subjects were classified as being intermediate metabolizers and 21 as being poor or intermediate metabolizers.

SNP	N	Genotype	n	Freq.(%)	95% CI	P-value
516G>T	48	GG	21	43.75	(29.8,58.7)	0.007
		GT	27	56.25	(41.3,70.2)	
		G	69	71.88	(61.6,80.4)	
		T	27	28.12	(19.7,38.4)	

Table:1 Genotype and allele frequencies of the CYP2B6 516G>T polymorphism

SNP	Genotype	Male	(%)	Female	(%)	P-value
516G>T	GG	17	(36.2)	4	(8.5)	1
	GT	22	(46.8)	5	(8.6)	
	G	56	(58.3)	13	(13.5)	1
	T	22	(22.9)	5	(5.2)	

Table:2 Allele and genotype frequencies of CYP2B6 516G>T per gender.

SNP	Genotype	Caucasian	(%)	Negroid	(%)	P-value
516G>T	GG	17	(35.4)	4	(8.3)	1
	GT	22	(45.8)	5	(10.4)	
	G	43	(52.44)	14	(17.07)	1
	T	19	(23.17)	6	(7.32)	

Table:3 Allele and genotype frequencies of CYP2B6 516G>T per races.

Haplotype	SNP 516G>T	SNP 785A>G	Metabolizer	n
*1/*4	GG	AG	intermediate	27
*1/*6	GT	AG	intermediate	21
*6/*6	GT	AG	poor	

Table 4: CYP2B6 haplotypes and their correspondence in terms of metabolism.

Conclusion

The study of the CYP2B6 gene variants is essential to provide information to complete the evalution of the impact of these polymorphisms in ARV.

There were no differences observed in the alellic and genotyping frequencies between genders and races.

Of the 48 patients, 27 were classified has having the CYP2B6 *1/*4 haplotype (intermediate metabolizers) and 21 as having CYP2B6 *1/*6 or *6/*6 haplotype (intermediate or poor metabolizers).

References

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