S-III-11

Effects of Clopidogrel and Itraconazole on the Disposition of Efavirenz in Relation to the CYP2B6 Genetic Polymorphisms in Healthy Subjects

Fen Jiang

Inje University College of Medicine

Aims: CYP2B6 play a crucial role in the disposition of numerous clinically important drugs. The individual diversity in its activity is well-known and this variation is attributed to polymorphisms of CYP2B6 and environmental factors such as inducers or inhibitors. It has been reported of more than 20 SNPs in CYP2B6 gene and their functional effects have been also addressed from in vitro and in vivo studies. Efavirenz is a first-line anti-HIV drug and metabolized mainly by CYP2B6 and CYP3A4 in vitro. Our objective was to evaluate the effect of clopidogrel and itraconazole, CYP2B6 and CYP-3A4 inhibitor respectively, on the pharmacokinetics of efavirenz in relation to CYP2B6*6 genotype.

Methods: We genotyped 374 Korean healthy subjects for CYP2B6*1 and *6 allele, and recruited 16 subjects with CYP2B6*1/*1(n=6), *1/*6(n=5), or *6/*6(n=4). We conducted clinical trial in a 3-phase, single-blinded, randomized, cross-over design. In each phase, subjects took a single oral dose (200 mg) of efavirenz with pre- or post-treatment of placebo, clopidogrel (75 mg/day, 4 days), or itraconazole (200 mg/day, 6 days) and blood and urine were collected for 120 hrs and 24 hrs. Assay of efavirenz and its metabolites was conducted using LC/MS/MS.

Results: Table 1.

Conclusions: Subject with CYP2B6*6/*6 showed the tendency of decreased oral clearance of efavirenz when compared with those with CYP2B6*1/*1 or *1/*6. The moderate effect of CYP2B6*6 genotype on efavirenz disposition seems to be magnified in the presence of clopidogrel and itraconazole, CYP2B6 and CYP3A4 inhibitor.

◈ Fen Jiang ◈