CYP3A5 MUTATION INCREASED RISK OF ERGOTISM IN CAFERGOT AND PROTEASE INHIBITORS DRUG INTERACTION

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Objectives: Cafergot is a common drug that used in migraine treatment. Cafergot causes vasoconstriction of both cerebral and peripheral arteries. Cafergot is metabolised by CYP3A enzyme. CYP3A4 and CYP3A5 are a common subfamily of CYP3A that is responsible for drug metabolism in human liver. Unlike *CYP3A4* gene, *CYP3A5* gene showed polymorphism effecting the expression of CYP3A enzyme. Therefore, *CYP3A5* mutation genotype patients may be increased risk of cafergot toxicity because of decreasing *CYP3A5* enzyme activity. Drug interactions between cafergot and protease inhibitor drugs (PIs) such as ritonavir, lopinavir, increase cafergot level and lead to ergotism. We reported four patients who had drug interactions between cafergot and PIs and presented with ergotism. Moreover, all of them showed mutation of *CYP3A5* gene.
Methods: Patient's medical records were reviewed in four patients who were admitted to Srinagarind Hospital, Faculty of Medicine, Khon Kaen University because of ergotism. *CYP3A5* genotype analysis was performed by real-time PCR technique.
Results: Three of them were HIV patients who received lopinavi/ritonavir as antiretroviral therapy. The last received lopinavi/ritonavir as prophylaxis of HIV infection after needle stick. Then, they received cafergot as migraine treatment. After taking cafergot for few days, they developed purple skin, painful and cold at distal part of both lower extremities. Physical examination showed peripheral cyanosis, poor capillary refill and weak peripheral pulses on distally on both lower extremities. Moreover, all of them had mutation of *CYP3A5*. Sodium nitropusside, heparin and nifedipine were administered. All of them had good recovery after treatment. ***Conclusions:*** *CYP3A5* mutation patients had decreased cafergot metabolism. This may be another factor that increases risk of cafergot toxicity in patients who concomitantly received cafergot and PIs. Therefore, not only drug interactions but also genetic polymorphism of *CYP3A5* causes ergotism in these patients.