Pharmacogenetics Study of Dapsone-Induced Severe Cutaneous Adverse Reactions and HLA Class I Alleles in Thai Patients

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Abstract : Dapsone (4, 4'-diaminodiphenyl sulfone, DDS) is broadly used for the treatment of inflammatory diseases and infections such as; leprosy, Pneumocystis jiroveci pneumonia in patients with HIV infection, neutrophilic dermatoses, dermatitis herpetiformis and autoimmune bullous disease. The severe cutaneous adverse drug reactions (SCARs) including, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) are rare but severe life-threatening adverse drug reactions. Dapsone is one of many culprit drugs induced SJS, TEN and DRESS. Notwithstanding, to our knowledge, there are no studies of the association of HLA class I alleles and dapsone-induced SCARs in non-leprosy Thai patients. This investigation was a prospective cohort study, which performed in a total of 45 non-leprosy patients. Fifteen patients of dapsone-induced SCARs were classified as following the RegiSCAR criteria, and 30 dapsone-tolerant controls were exposed to dapsone more than 6 months without any evidence of cutaneous reactions. The genotyping of HLA-A, -B and –C were performed using sequence-specific oligonucleotides (PCR-SSOs). The Ethics Committee of Ramathibodi hospital, Mahidol University, approved this study. Among all HLA class I alleles, HLA-A*24:07, HLA-B*13:01, HLA-B*15:02, HLA-C*03:04 and HLA-C*03:09 were significantly associated with dapsone-induced SCARs (OR = 10.55, 95% CI = 1.06 – 105.04, p = 0.0360; OR = 56.00, 95% CI = 8.27 – 379.22, p = 0.0001; OR = 7.00, 95% CI = 1.17 – 42.00, p = 0.0322; OR = 6.00, 95% CI = 1.24 – 29.07, p = 0.0425 and OR = 17.08, 95% CI = 0.82 – 355.45, p = 0.0321, respectively). Furthermore, HLA-B*13:01 allele had strong association with dapsone-induced SJS-TEN and DRESS when compared with dapsone-tolerant controls (OR = 42.00, 95% CI = 2.88 – 612.31, p = 0.0064 and OR = 63.00, 95% CI = 7.72 – 513.94 and p = 0.0001, respectively). Consequently, HLA-B*13:01 might serve as a pharmacogenetic marker for screening before initiating the therapy with dapsone for prevention of dapsone-induced SCARs.