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Association of HLA-B*1502 allele and carbamazepine-induced severe adverse cutaneous drug reaction among Asians, a review

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Abstract

Strong association between HLA B*1502 and carbamazepine-induced Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) was demonstrated among Han Chinese in 2004. Studies from Europe showed that the HLA B*1502 is not a universal marker for SJS/TEN, but is ethnicity specific for Asians. Reports across Asia has shown that the prevalence of HLA B*1502 is high among Han Chinese (5-15%), Malays (12-15%), and Thais (8-27%), but low among Japan, Korea, Sri Lanka, and most ethnic groups in India. Other than Han Chinese, the association between HLA B*1502 and carbamazepine-induced SJS-TEN is also seen among the Thais and Malay. There is urgent need for further studies to determine the prevalence of SJS/TEN, and HLA B*1502 in the various ethnic groups in Asia, and its association with carbamazepine-induced SJS-TEN in each of these ethnic groups. In view of the significant morbidity and mortality in SJS-TEN, facilities should be developed to allow for screening of HLA B*1502 before carbamazepine is prescribed to the Hans Chinese, Malays and Thais. For those who experience no adverse cutaneous reaction after 3 months use of carbamazepine, the risk of SJS/TEN is low, and the drugs can be continued.

INTRODUCTION

In 2004, Chung *et al*[1] from Taiwan reported from their Han Chinese patients, a strong association between carbamazepine (CBZ)-induced Stevens-Johnson syndrome (SJS) and HLA-B*1502. The HLA-B*1502 allele was seen in all 44 patients with CBZ-SJS, only 3% of CBZ-tolerant patients, and 8.6% of the normal population. The same group later expanded the study, and showed that the strong association of CBZ is with severe cutaneous drug reaction, i.e. SJS and toxic epidermal necrolysis (TEN), but not with the milder maculopapular eruption and hypersensitivity syndrome.[2] Lonjou *et al* reported from their 12 European patients with CBZ-induced SJS/TEN, that only 4 had a HLA-B*1502, and all the 4 had an Asian ancestry.[3] The study thus indicates that HLA-B*1502 is not a universal marker for CBZ-induced SJS/TEN, but is ethnicity specific. The US Food and Drug Administration (FDA) has published an alert to healthcare professionals on the use of CBZ to Asians.[4] As CBZ-induced adverse skin reaction is a relatively common clinical problem among some Asians with potential fatal outcome, this paper aims to review the results of study to date, the important clinical issues to be clarified, and guidelines to physicians in their clinical practice in Asia.

SEVERE ADVERSE CUTANEOUS DRUG REACTION

Severe adverse cutaneous drug reaction (ACDR), for example SJS and TEN are life-threatening skin reactions to medications. TEN is an acute dermatologic disease, characterized by widespread erythematous macules and targetoid lesions; full-thickness epidermal necrosis, at least focally; and involvement of more than 30% of the cutaneous surface. SJS may have full-thickness epidermal necrosis, but with lesser detachment of the cutaneous surface; and mucous membrane involvement.[5-6]

Maculopapular exanthema and hypersensitive skin syndrome are other spectrum of cutaneous drug reactions. Maculopapular exanthema is characterized by cutaneous fine pink macules and papules, lesions which usually fade within 1–2 weeks following cessation of drug treatment. Hypersensitive skin syndrome is characterized by multi-organ involvement (e.g. hepatitis and nephritis) accompanied by systemic

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