Should patients of Thai, Han Chinese and Hong Kong Chinese origin be tested for HLA-B*1502 allele prior to phenytoin treatment?

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Background

Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) reactions (Fig. 1) are potentially fatal adverse drug reactions.

- SJS/TEN reactions are ten times higher in the Thai, Han Chinese and Hong Kong Chinese (T/HC/HKC) due to the presence of the human leukocyte antigen HLA-B*1502.
- HLA-B*1502 presents in 6.1%/9%/7.2% of the T/HC/HKC population respectively.
- Carbamazepine (CBZ) induced SJS/TEN is greater in patients with HLA-B*1502 allele.
- Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) advise testing for HLA-B*1502 prior to initiation of CBZ in the T/HC/HKC population.
- MHRA and FDA only advise avoiding Phenytoin (PHT) if the patient is known to have HLA-B*1502 and do not advise routine testing for the allele.
- The increasing evidence regarding the link between HLA-B*1502 and PHT-induced SJS/TEN may alter the management of patients of T/HC/HKC origin.

Objective

Assess the association of HLA-B*1502 and PHT-induced SJS/TEN in patients of T/HC/HKC origin.

Study Design

- Literature search on PubMed and ScienceDirect databases until October 2014.
- Search words “phenytoin”, “HLA-B*1502”, “Steven-Johnson Syndrome” and “Toxic Epidermal Necrolysis”
- Other articles used were those cited in papers identified via the literature search
- Analysis was restricted to systematic reviews and meta-analyses to establish the odds ratio (OR).

Results and discussion

In total, 45 cases and 217 controls assessed. There was an increased risk of PHT-induced SJS/TEN in patients with HLA-B*1502 allele compared to those that did not possess the allele.

<table>
<thead>
<tr>
<th>Continent</th>
<th>Population/Ethnicity</th>
<th>HLA-B*1502</th>
<th>Sample size</th>
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<tbody>
<tr>
<td>Asia</td>
<td>Thailand</td>
<td>0.085</td>
<td>142</td>
</tr>
<tr>
<td>China</td>
<td>Southern Han</td>
<td>0.073</td>
<td>264</td>
</tr>
<tr>
<td>China</td>
<td>Northern Han</td>
<td>0.019</td>
<td>105</td>
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<tr>
<td>Europe</td>
<td>Wales, White</td>
<td>0.000</td>
<td>1798</td>
</tr>
<tr>
<td></td>
<td>Northern Ireland</td>
<td>0.000</td>
<td>1000</td>
</tr>
</tbody>
</table>

There is strong evidence associating PHT-induced SJS/TEN and individuals with HLA-B*1502 of T/HC/HKC origin. The incidence of SJS/TEN could be reduced by routine testing for HLA-B*1502 allele in patients of T/HC/HKC origin prior to initiation of phenytoin, and thus one can avoid the use of phenytoin treatment in this subset of patients.

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