Haptoglobin genotype and aneurysmal subarachnoid hemorrhage

Individual patient data analysis

Ben Gaastra, MRCS, Dianxu Ren, PhD, Sheila Alexander, PhD, et al.

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Study objective and summary result
This study tested the hypothesis that haptoglobin genotypes influence outcomes after aneurysmal subarachnoid hemorrhage (aSAH), and it found that haptoglobin genotypes were not associated with post-aSAH outcomes.

What is known and what this paper adds
Past studies, including a meta-analysis, have suggested that haptoglobin genotypes are associated with post-aSAH outcomes, but the results have been inconsistent. This study provides strong evidence against any such association.

Design, size, and duration
In January 2017, this study searched PubMed and the Web of Science for previous studies that tested for associations between haptoglobin genotypes and outcomes, as assessed with the modified Rankin Scale (mRS) or the Glasgow Outcome Scale (GOS), at 1, 3, or 6 months post-aSAH timepoints. This study also used the authors’ professional networks to identify unpublished studies with suitable data. This study extracted individual patient level data (IPLD) from the selected studies. Because 2 haptoglobin alleles (i.e., HP1 and HP2) exist in humans, each patient’s haptoglobin genotype was categorized as HP1-1, HP1-2, or HP2-2. This study defined favorable outcomes as scores of 4–5 on the GOS or 0–2 on the mRS. This study used generalized estimating equation models with a logit link to determine whether haptoglobin genotypes were associated with favorable post-aSAH outcomes.

Participants and setting
This study found 5 published studies and 6 unpublished studies eligible for inclusion in the IPLD meta-analysis. These 11 studies yielded IPLD for 939 individuals and were conducted in the USA, the UK, Japan, and Italy.

Primary outcome measures
The primary outcomes were associations between haptoglobin genotypes and post-aSAH outcomes.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds ratio (95% confidence interval) for unfavorable post-aSAH outcomes</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP2-2 vs HP2-1 &amp; HP1-1</td>
<td>0.997 (0.672–1.421)</td>
<td>0.905</td>
</tr>
<tr>
<td>HP2-2 vs HP1-1</td>
<td>0.752 (0.429–1.321)</td>
<td>0.322</td>
</tr>
<tr>
<td>HP2-1 vs HP1-1</td>
<td>0.814 (0.470–1.410)</td>
<td>0.462</td>
</tr>
<tr>
<td>HP2-2 vs HP2-1</td>
<td>1.021 (0.684–1.524)</td>
<td>0.921</td>
</tr>
<tr>
<td>HP2-2 &amp; HP2-1 vs HP1-1</td>
<td>0.776 (0.461–1.305)</td>
<td>0.339</td>
</tr>
</tbody>
</table>

Main results and the role of chance
The meta-analysis revealed no associations between haptoglobin genotypes and post-aSAH outcomes.

Bias, confounding, and other reasons for caution
This study had a retrospective design and might have been subject to selection bias in favor of patients with delayed cerebral ischemia and a lower coiling to clipping ratio. This study lacked complete data from all sites for some covariates relevant to post-aSAH outcomes.

Generalizability to other populations
This study’s reliance on data from 4 high-income countries may limit the generalizability of the results.

Study funding/potential competing interests
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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.