Table 2. Aspirin Dose and Intracranial Hemorrhage in Double-Blind Clinical Trials

<table>
<thead>
<tr>
<th>Daily aspirin dose</th>
<th>None</th>
<th>30 mg</th>
<th>75 mg</th>
<th>300 mg</th>
<th>1,200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK-TIA¹</td>
<td>2</td>
<td>...</td>
<td>...</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Dutch TIA²</td>
<td>...</td>
<td>13</td>
<td>...</td>
<td>15*</td>
<td>...</td>
</tr>
<tr>
<td>SALT³</td>
<td>3</td>
<td>...</td>
<td>8</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>USPHS⁴</td>
<td>12</td>
<td>...</td>
<td>...</td>
<td>23*</td>
<td>...</td>
</tr>
</tbody>
</table>

*283 mg in Dutch TIA trial; 325 mg every other day in USPHS.

mg/day. It is problematic whether this difference in antithrombotic effect, based on microvascular or venous bleeding, is relevant in ischemic stroke prevention.

Pooling data from several trials, aspirin appears to double the risk of intracerebral hemorrhage in patients with cerebrovascular disease (Table 2), although this has not been statistically significant in individual cerebrovascular trials. Oddly, this appears to occur with doses as low as 75 mg/day. The data relating the dose of aspirin to the frequency of intracerebral hemorrhage include fewer outcome events than those pertaining to non-GI minor hemorrhage, but there appears to be no difference between 30 mg and 1,200 mg/day on the relative risk of brain hemorrhage.

Is there really an important difference in efficacy between doses of aspirin in patients with cerebrovascular disease? The in vivo effect on non-GI minor bleeding would support this idea, yet the increase in intracerebral hemorrhage (albeit with fewer end points for analysis) is seemingly not dose dependent. The optimal dose of aspirin for prevention of stroke is a continuing controversy, “a riddle wrapped in a mystery inside an enigma.”

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References

Response
Drs. Hart and Pearce draw attention to the relatively low rate of epistaxis and bruising in patients treated with 30 mg aspirin (Dutch TIA Trial) or with placebo (UK-TIA Trial) compared with those using 283 or 300/1,200 mg, respectively. We wish to point out several pitfalls in the interpretation of these selected side effects.

1. Data-dependent subgroup analysis can be highly misleading. For instance, in the ISIS-2 study, aspirin failed to reduce mortality after acute myocardial infarction in those patients who had Gemini or Libra as their astrological birth sign. Not only have gastrointestinal hemorrhages been excluded from the numbers given here, but cerebral hemorrhages are analyzed separately and other hemorrhages have been omitted.

2. Comparing “similar” subgroups is even more tricky; the procedures for detecting and auditing minor hemorrhages in trials of antithrombotic treatment usually are much less strictly defined than those for primary outcome events. Table 1 of the preceding letter illustrates this remarkably well: the 21 bruises and nose-bleeds in the 300-mg group of the UK-TIA trial correspond with six per 1,000 patient-years against 18 per 1,000 patient-years for the 70 similar bleeds in the 283-mg group of the Dutch TIA Trial. The difference is statistically significant, but it is far from us to attribute this to the 17-mg difference between the doses nor to differences between Englishmen and Dutchmen.

3. The answer to the question “whether this difference in antithrombotic effect, based on microvascular or venous bleeding, is relevant in ischemic stroke prevention” is obvious from the efficacy analysis of the Dutch TIA trial: it is not.

Everyone is entitled to his own mysteries, but is not the proposed link between side effects and efficacy a bit of mystification?

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Stoke Risk Factors in an African Population: A Report From Sierra Leone

In an attempt to gather the most basic information on stroke risk factors in this population, the records of 87 patients with the clinical diagnosis of stroke admitted to the main hospital in the city’s capital Freetown were reviewed. These were nonselected patients hospitalized over a 2-year period in one of the medical units of the hospital. All the patients were seen by the author. No computed tomographic scanning facilities were available, and the distinction between hemorrhagic and ischemic stroke was not made. Routine biochemistry tests, chest x-ray, and electrocardiography were performed. Hypertension was defined as blood pressure ≥160/95 on at least two occasions 48 hours after admission.

The study group comprised 57 males (65.5%) and 30 females (34.5%), giving a sex ratio of almost two males: one female. The mean age of the sample population was 50.9 years, and the peak age prevalence was in the sixth decade; 18.4% of patients were under 40 years of age. Forty patients had a right hemiplegia and 36 left hemiplegia. The rest had either brain stem stroke, isolated aphasia, or were too deeply comatose for their pattern of weakness to be determined. Thirteen patients died during admission, giving a mortality rate of 14.9%. In fatal cases, the average age was 64.6 years, compared with 48.4 years for survivors. Ten patients aged 70 years and above had a fatal outcome.

Hypertension was present in 59 of the cases (68%). In about half of these the diastolic pressure exceeded 120 mm Hg. When stratified by age, no patient under the age of 30 was hypertensive. The peak age group for hypertension was 40–59 years of age.
Stroke risk factors in an African population: a report from Sierra Leone.

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