Letters to the Editor

Table 1. Frequency of Hemorrhagic Strokes in Placebo-Controlled Clinical Trials of Effectiveness of Aspirin for Prevention of Stroke

<table>
<thead>
<tr>
<th>Reference/Author/Country</th>
<th>Dose (mg/day)</th>
<th>% Male</th>
<th>Months of follow-up</th>
<th>Age (yr)</th>
<th>No. hemorrhagic strokes/No. subjects randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/Atrial Fibrillation Study Group+/USA</td>
<td>325</td>
<td>71</td>
<td>24</td>
<td>67</td>
<td>1/517 0/528</td>
</tr>
<tr>
<td>7/UK-TIA Study Group 8/Swedish Cooperative Study</td>
<td>1,500</td>
<td>62</td>
<td>24</td>
<td>68</td>
<td>3/253 2/252</td>
</tr>
<tr>
<td>9/Sorensen et al/Denmark</td>
<td>1,000</td>
<td>73</td>
<td>25±</td>
<td>59</td>
<td>1/101 1/102</td>
</tr>
<tr>
<td>10/Bousser et al/France</td>
<td>300</td>
<td>70</td>
<td>36</td>
<td>63</td>
<td>2/198 2/204</td>
</tr>
<tr>
<td>11/Fields et al/USA</td>
<td>1,500</td>
<td>66</td>
<td>24</td>
<td>≥45</td>
<td>1/88 0/90</td>
</tr>
<tr>
<td>12/Gent et al/Canada</td>
<td>1,400</td>
<td>NE</td>
<td>42</td>
<td>NE</td>
<td>0/143 0/137</td>
</tr>
<tr>
<td>13/Reuter and Dorndorf#W. Germany</td>
<td>1,500</td>
<td>65</td>
<td>24</td>
<td>NE</td>
<td>0/60 0/60</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21/2,981 8/2,187</td>
</tr>
</tbody>
</table>

Age, mean age unless otherwise indicated; NE, not estimable.
*Warfarin group excluded.
†Two doses of aspirin.
‡Median length of follow-up.
§Group with both aspirin and dipyridamole excluded.
||Post surgical treatment groups excluded.
||Groups with sulfinpyrazone excluded.
||Number of hemorrhagic strokes inferred from article.

Aspirin and Hemorrhagic Stroke

To the Editor:

We have noted an increasing rate of hemorrhagic stroke in the Province of Quebec, Canada,1 and are concerned that this rise may be due in part to increased consumption of aspirin.

Recently, there has been much discussion about the use of aspirin for the primary prevention of myocardial infarction, arising mainly from findings from two recent clinical trials.2,3 Not only were these two studies discordant on the degree to which aspirin was associated with hemorrhagic strokes, but they also differed on the extent to which aspirin was associated with hemorrhagic strokes. In the study of British physicians,3 there was no difference in number of hemorrhagic strokes in the group taking aspirin compared with the group avoiding aspirin (relative risk [RR]=1.1). In the American Physicians' Health Study,2 the group taking aspirin experienced twice as many hemorrhagic strokes as those taking a placebo (23 cases versus 12 cases; RR=2.14, p<0.06).

Estimates of the risk of hemorrhagic stroke associated with the use of aspirin can also be gleaned from the many clinical trials evaluating the effectiveness of aspirin for the primary and secondary prevention of myocardial infarction and stroke. Clinical trials for the prevention of myocardial infarction, for the most part, did not enumerate hemorrhagic strokes as separate events and thus do not permit an opportunity to assess risk. The studies on the prevention of stroke do provide this opportunity, but in no one trial were there enough hemorrhagic events to raise concern; taken collectively, the possibility of an increased risk emerges.

In Table 1, we have compiled the findings on the occurrence of hemorrhagic stroke events from eight placebo-controlled randomized clinical trials of aspirin for the prevention of stroke. There were a total of 21 hemorrhagic strokes occurring among the 2,981 persons who were randomized to receive aspirin compared with seven hemorrhagic strokes among the 2,187 persons randomized to placebo (RR=1.93, 95% confidence interval 0.82–4.54). The confidence interval was calculated from the estimate of standard error derived using logistic regression, which modeled the logarithm of the odds of hemorrhagic stroke by assignment to aspirin or placebo groups.

Owing to the large variability associated with this estimate of risk and to potential biases we were unable to measure or control, these data do not provide convincing evidence that aspirin is associated with increased risk of hemorrhagic stroke. However, because of the increasing prevalence of aspirin use and the twofold excess risk estimated from these clinical trials, it might be prudent to consider testing the hypothesis that aspirin use is a risk factor for hemorrhagic stroke.

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References
In our experience, the survival rate of lacunar patients was 4.7/100 patients/year, much lower than that of survivors from cerebral infarction.

An excess of mortality was observed in patients with multiple lacunes suffering from a pseudodubellar syndrome, with poor functional recovery, poorly controlled arterial hypertension, and age >65 years.

"The common denominator for the definition of lacune, whether used by a pathologist, clinician, or radiologist, is that it's small." Thus the term lacune can be replaced by the label "small stroke," or "small, deep stroke." "Confusion has come to clinical practice when the adjective form is used, as in 'lacunar disease,' 'lacunar state,' 'lacunar syndrome,' 'lacunar infarction,' and 'lacunar stroke,' often with the implication that these small infarcts are caused by hypertension and small-vessel disease (the 'lacune hypothesis')."1

I believe that lacune is only a pathological term; however, the definition "lacunar syndrome" is customarily applied to clinical pictures such as sensory strokes, pure motor hemiplegias, ataxic hemiparesis, and dysarthria-clumsy hand syndromes, in relation to small, low-density areas, as shown by CT scan. Moreover, syndromes brought about by lacunes also include reversible ischaemic attacks (transient ischaemic attack or reversible ischaemic neurologic disease).4

On the other hand, the role of lacunes in bringing about dementia is debated, as is the role of multiple infarctions.9

Should the so-called lacunar syndrome be considered a misleading label, and can we substitute the term "small, deep infarction syndrome" for this term? Obviously, these small, deep strokes (how small? how deep?) still exhibit different clinical features and progressions than larger infarctions.

Like Toole's definitions10 of syndromes of the carotid and vertebrobasilar arteries and their branches, I would suggest the label of "syndrome of the small intracerebral arteries" for lacunar syndrome. Indeed, the definition and classification of cerebrovascular disease, mainly with respect to transient ischemic attacks and lacunes, need a thorough revision.

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References


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