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The MATCH Study Results in the Context of Secondary Stroke Prevention

Marc Fisher, MD; Antonio Davalos, MD, PhD

The performance of randomized clinical trials provides evidence-based medical information to clinicians and impacts on day-to-day treatment decisions. Many secondary stroke prevention trials over the past 4 decades have provided much useful information concerning the efficacy or lack thereof of different therapies for reducing recurrent stroke risk. For platelet antiaggregants, placebo-controlled trials are no longer justified and comparator trials evaluating drug combinations in comparison to monotherapy are appropriate. The MATCH trial evaluated the efficacy and safety of combined clopidogrel–aspirin therapy to clopidogrel alone in high-risk patients with completed stroke or transient ischemic attack who also had 1 or more of 5 additional risk factors. The combined endpoint of ischemic stroke, myocardial infarction, vascular death, or recurrent hospitalization for an ischemic event was used. The study demonstrated an insignificant trend for greater efficacy with the combination therapy on the primary endpoint, but a highly significant increased risk for life-threatening bleeding side effects.

Because of the importance of this study, we asked for critiques from both North American and non-North American perspectives. Dr Caplan invokes a familiar theme that the precise nature of the arterial lesion was not well-characterized in MATCH, similar to the situation in other platelet antiaggregant trials and the recently reported Warfarin–Aspirin Recurrent Stroke Study (WARRS). He additionally points out that >50% of the patients in MATCH were classified as small vessel in subtype, a figure similar to the WARRS study. This is a disproportionate number when compared with general stroke registries that likely affected the power and generalizability of these trials. Dr Caplan concludes that comparing clopidogrel–aspirin to clopidogrel alone and not aspirin alone leaves unanswered questions concerning the effectiveness and safety of the combination in comparison to the currently most widely used platelet antiaggregant in cerebrovascular patients, aspirin. Ongoing studies are addressing this issue.

Drs Amarenco and Donnan provide a different perspective on the MATCH trial and its results. They emphasize that the study population was skewed toward multiple risk factors because of the requirement for high-risk patients and that 68% had diabetes mellitus, which is a very high percentage. They also raise concerns about the substantial percentage of small-vessel disease patients in the study and the impact on outcome events. They conclude that the MATCH results for a trend toward greater efficacy of the combination of clopidogrel plus aspirin and the significant risk of life-threatening bleeding can only be applied to a cerebrovascular population similar to that included in the study. They support the continuation of ongoing studies that are evaluating this combination in comparison to aspirin or warfarin and suggest that clinicians “exercise caution” in prescribing clopidogrel plus aspirin to patients with diabetic cerebrovascular disease.

The critiques of the MATCH study provided by Dr Caplan, and Drs Amarenco and Donnan are both insightful and somewhat disparate in their conclusions. Until proven no more risky than aspirin alone or the combination of aspirin/extended-release dipyridamole, the combination of clopidogrel/aspirin cannot, in our opinion, be recommended for use in routine clinical practice for cerebrovascular disease patients. An exception might be considered for cerebrovascular disease patients undergoing a cardiac procedure such as stenting/angioplasty in which the CURE study suggests benefit, but in this setting the combination of clopidogrel/aspirin should likely be used for months and not indefinitely. The efficacy and safety of clopidogrel/aspirin in cerebrovascular disease patients need to be explored in additional clinical trials and some are already ongoing. However, the data and safety-monitoring boards of such trials need to be particularly vigilant concerning life-threatening bleeding side effects to avoid continuing to accrue patients if a similar bleeding risk emerges as was observed in the MATCH study.

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