Treatment Effect of Clopidogrel Plus Aspirin within 12 Hours of Acute Minor Stroke or Transient Ischemic Attack

Acute minor stroke or transient ischemic attack (TIA) events often are warning signs of a possible pending disabling ischemic stroke and increase the risk of new stroke events, most of which occur within the initial hours and days after symptom onset.[1]

Given the short therapeutic time window, treatment should be started immediately to reduce the risk of new stroke events. Antiplatelet therapy initiated within 48 hours of symptom onset in ischemic stroke patients decreased their risk of new stroke events. [2]

The Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial and another trial demonstrated that patients with high-risk acute minor stroke or TIA who were treated with clopidogrel and aspirin within 24 hours of symptom onset had fewer subsequent stroke events than did those taking aspirin alone. [3]

CHANCE trial conducted in July 4 2013, is a prospective multicenter double‐blind randomized placebo‐controlled trial conducted at 114 centers in China. The trial compared the combination therapy of clopidogrel and aspirin (clopidogrel at an initial dose of 300 mg, followed by 75 mg/d for 90 days, plus aspirin at a dosage of 75 mg/d for the first 21 days) versus placebo plus aspirin (75 mg/d for 90 days) in 5170 patients who were 40 years or older and able to start the study drug within 24 hours after the onset of minor ischemic stroke. All participants received open‐label aspirin at a clinician‐determined dose of 75 to 300 mg on the first day). [3]

In March 21, 2016, a sub analysis study of the CHANCE trial, lasted for 21 days**,** was published and it was mainly limited to a prespecified group of patients randomized within 12 hours to either the combination of clopidogrel plus aspirin or aspirin alone, analyzed the benefits and safety associated with the combination therapy of clopidogrel and aspirin among minor stroke or transient ischemic attack patients treated within 12 hours. Of the 5170 patients enrolled in the CHANCE trial, 2573 patients were divided into clopidogrel–aspirin group (1293 patients) and aspirin alone group (1280 patients). [4]

The primary outcome of our study was ischemic stroke during 90 day follow up. Secondary end event of efficacy was a new clinical vascular event (ischemic stroke, hemorrhagic stroke, myocardial infarction, or vascular death). The primary end event of safety was a moderate to severe bleeding event. During 3 months follow up of all patients randomized within 12 hrs of TIA, and **in terms of Efficacy**, 124 patients in the clopidogrel–aspirin group, experienced an ischemic stroke compared with 158 patients in the aspirin group (P=0.02). Also, the clopidogrel–aspirin treatment was more likely than the aspirin alone to reduce the risk of recurrent ischemic stroke (P=0.03) but not progressive ischemic stroke (P=0.28). [4]

The composite outcome of vascular events occurred in 127 patients in the clopidogrel–aspirin group and 165 patients in the aspirin group (*P*=0.01). One cardiovascular death occurred in the clopidogrel–aspirin group and 2 occurred in the aspirin group (*P*=0.57). In terms of **Safety,** 4 of 2573 patients treated within 12 hours of symptoms onset had moderate or severe bleeding events during the 3 month follow up period. Zero patient of the clopidogrel–aspirin group, experienced a severe bleeding event compared with one patient in the aspirin group. For any bleeding event, it occurred in 26 in the clopidogrel–aspirin group and 18 in the aspirin group (*P*=0.39). [4]

In conclusion, patients treated within 12 hours, the combination of clopidogrel and aspirin was more effective than aspirin alone in reducing the risk of recurrent ischemic stroke during the 90-day follow-up and did not increase the hemorrhagic risk. Also, because the highest risk period for new stroke events was during the early hours and days after the initial ischemic event, aggressive antiplatelet therapy among patients with minor stroke or TIA should be administrated as early as possible.

References:

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