Early dual antiplatelet therapy after minor stroke: Does it take two to tango?

CLINICAL QUESTION

In acute non-cardioembolic minor ischemic stroke or transient ischemic attack (TIA), does adding a second antiplatelet (like clopidogrel or ticagrelor) to ASA reduce recurrent stroke?

BOTTOM LINE

Compared to ASA alone, clopidogrel plus ASA reduced the risk of stroke from 8.2% to 5.5% but increased the risk of major bleeds from 0.6% to 1.2% at 21 days. Continuing clopidogrel beyond 21 days increased major bleeds without reducing strokes. There is no evidence that ticagrelor is more efficacious in reducing stroke than clopidogrel.

EVIDENCE

- Clopidogrel + ASA versus ASA: Time analysis from meta-analysis of 3 randomized controlled trials (RCTs), 10,447 patients:
  - Clopidogrel (300-600mg on day 1, then 75mg/day) plus ASA within 12-24 hours of onset of minor ischemic stroke or high-risk TIA versus ASA alone for 21-90 days, followed by single antiplatelet.
  - At 21 days:
- Ischemic stroke: 5.5% versus 8.2% (ASA), number needed to treat (NNT)=38.
- Major bleed: 1.2% versus 0.6% (ASA) (number needed to harm [NNH]=167)
  - On days 22-90:1,2
    - Ischemic stroke: No difference.
    - Major bleed: 0.6% versus 0.3% (ASA), NNH=334.
- Ticagrelor + ASA versus ASA: One RCT, 11,016 patients:3
  - Started ticagrelor (180mg on day 1, then 90mg twice daily) plus ASA within 24 hours of mild-moderate ischemic stroke or TIA versus ASA alone, continued for 30 days.
    - Ischemic stroke: Ticagrelor + ASA 5.0%, ASA 6.3%, NNT=84.
    - Moderate-severe bleed: 0.65% versus 0.2%, NNH~200
      - Intracranial hemorrhage: 0.36% versus 0.11%, NNH~330.
- No significant differences in disability or death between dual and single antiplatelet.1

**CONTEXT**
- “Minor” stroke defined based on the National Institutes of Health Stroke Scale ≤3-5.1,4
- Cardioembolic strokes (e.g. related to atrial fibrillation) are treated differently.5
- Recurrent stroke risk highest within ~2 weeks of event.1,2,4
  - Guidelines recommend clopidogrel + ASA for 21 days in patients with acute non-cardioembolic minor ischemic stroke.5
- Clopidogrel or ticagrelor alone have similar efficacy to ASA alone in minor-moderate ischemic non-cardioembolic stroke.6,7
- In acute coronary syndromes, ticagrelor + ASA causes more major bleeding and dyspnea (NNH 16) than clopidogrel + ASA.8
- Costs per 90 days: ASA $5, clopidogrel $40, ticagrelor $320.9

**REFERENCES**


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