INTRODUCTION

• Treatment with an antiplatelet agent is recommended for the secondary prevention of stroke and other cardiovascular events in patients with non-cardioembolic ischemic stroke.¹
• The effectiveness of aspirin for the reduction in risk of ischemic stroke has been studied in large randomized clinical trials and meta-analyses,² ³ but relative effectiveness among other antiplatelet therapies has not been established.⁴

Clopidogrel alone or in combination with aspirin has demonstrated a favorable benefit-risk profile in patients with acute stroke;⁵ however, there is limited data comparing clopidogrel alone with aspirin.⁶ Better understanding of the benefit of clopidogrel compared to aspirin will provide useful information for healthcare providers and patients to guide selection of optimal antiplatelet treatment for secondary prevention after acute ischemic stroke.

AIM

To conduct a systematic literature review to compare the efficacy and safety of clopidogrel vs aspirin monotherapy in patients with acute ischemic stroke.

METHODS

• A standardized review protocol was used to define the eligibility criteria for the search and screening of references using the PICO(TSS) framework, which identifies the population, interventions, comparisons, outcomes, timing, setting, and study designs of interest (Table 1).

• MEDLINE® (via PubMed), Embase (via OVID) and Cochrane Central Register of Controlled Trials (via Wiley) were searched. Language (English), publication date (from inception to May 2017) and subject (humans) limits were applied in each database.

• Conference proceedings from the American College of Cardiology, European Society of Cardiology, American Heart Association, and the European Heart Association congresses (2015 to May 2017) were also reviewed.

• Data extraction was conducted using the Digital Outcome Conversion (DOC®) Data version 2.0 software platform (Doctor Evidence, LLC, Santa Monica, CA, USA) and its universal electronic extraction form, based on a standardized data configuration protocol. Each collected data point was extracted by two highly trained and proctored evidence analysts. All terms (characteristics and outcomes) were collected as reported in each paper and synonyms were bound before analysis using the DOC® Ontology System.

• Efficacy outcomes included all recurrent stroke (total ischemic and hemorrhagic), recurrent ischemic stroke, major adverse cardiovascular and cerebrovascular events (MACCE), and all-cause mortality. MACCE was comprised of the following outcomes: recurrent stroke, myocardial infarction, unstable angina, coronary revascularization, aortic aneurysm rupture, peripheral artery disease, vascular death and sudden death. Safety outcomes included intracranial hemorrhage.

• A pairwise meta-analysis was performed using the DerSimonian-Laird random effects model to estimate risk ratios and 95% confidence intervals. Heterogeneity was assessed using the I² statistic.

RESULTS

• The search in databases and relevant congresses resulted in 9624 potentially relevant references after duplicates were removed. Of that, 9520 records were retained before title and abstract screening and an additional 98 based on review of the full text (see Figure 1 for the flow of studies through the review).

• Six studies (one randomized controlled trial, two prospective observational and three retrospective observational) met eligibility criteria and were included in the analysis (see Table 2 for overview of the included studies). Among 35,633 patients, 42.8% (n=15,238) received clopidogrel and 57.2% (n=20,395) received aspirin. Follow-up in studies ranged from 3 months to over 3 years.

• In two studies reporting the total number of ischemic and hemorrhagic stroke, patients receiving clopidogrel were 34% less likely to experience another stroke compared to aspirin (127 of 732 clopidogrel patients versus 673 of 2380 aspirin patients; risk ratio 0.66; 95% CI 0.53-0.81, p<0.001) (Figure 2).

• The risk of recurrent ischemic stroke was 19.9% lower for clopidogrel versus aspirin (risk ratio 0.80; 95% CI 0.61-1.07), this result was not statistically significant (Figure 3).

• A statistically significant risk reduction of 28.5% for MACCE was found for clopidogrel versus aspirin (risk ratio 0.72; 95% CI 0.53-0.97, p<0.05) (Figure 4). Significant heterogeneity was observed.

• The risk of all-cause mortality was reduced by 8.3% for clopidogrel versus aspirin (risk ratio 0.92; 95% CI 0.85-1.00), but the result was not statistically significant (Figure 5).

• The risk of intracranial hemorrhage was 31.9% lower for clopidogrel versus aspirin, this result was not statistically significant (risk ratio 0.68; 95% CI 0.44-1.08) (Figure 6).

REFERENCES


DISCLOSURES

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