

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Choice of antiplatelet agent for secondary prevention of stroke

The risk of recurrent stroke is as high as 43% over 10 years. Antiplatelet therapy is an accepted strategy for reduction in this risk. The common choices are aspirin, aspirin plus extended release Dipyridamole (ASA-ESDP), and clopidogrel. When selecting an antiplatelet there should be consideration of co-morbidities (especially acute coronary disease), tolerance, and recurrence of stroke while on an antiplatelet.

Aspirin plus Dipyridamole (ASA-ESDP)

Trial evidence (ESPS 2 and ESPRIT) shows that aspirin alone reduces the risk of stroke and that there is an additive risk reduction when aspirin is combined with modified release dipyridamole. Headache associated with the dipyridamole component leads to more discontinuations in therapy than with aspirin alone.

Clopidogrel

In the CAPRIE study the annual combined risk of ischaemic stroke, MI and vascular death was 5.32% with clopidogrel, versus 5.83% with aspirin. This was a small difference in absolute risk reduction favouring clopidogrel, suggesting that there is another reasonable option when patients have a recurrent stroke while taking aspirin.

Clopidogrel plus aspirin

The combination of clopidogrel & aspirin is not recommended for secondary prevention of stroke in patients who do not have acute coronary disease or a recent coronary stent. In the secondary prevention trials MATCH and CHARISMA, efficacy of combined clopidogrel and aspirin was not significantly different from clopidogrel alone (MATCH study) or aspirin alone (CHARISMA study). There was a significant excess in life threatening, major & minor bleeding with the combination compared to clopidogrel alone, & a significant increase in moderate bleeding compared to aspirin alone.

Clopidogrel versus ASA-ESDP

The first direct comparison of ASA-ESDP versus clopidogrel for secondary prevention of stroke was published in 2008. The Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) study was designed to test non-inferiority of ASA-ESDP compared to clopidogrel. After a mean duration of 2.5 years the primary outcome of recurrent stroke of any type was close to equivalent between groups, and statistical analysis was unable to demonstrate non-inferiority of ASA-ESDP to Clopidogrel. The number of patients with fatal or disabling strokes was similar in the 2 groups:

	ASA-ESDP	Clopidogrel	
Major haemorrhagic events	4.1%	3.6%	
Intracranial haemorrhage	1.4%	1%	P=0.006
Premature discontinuation of drug	29.1%	22.6%	P,0.001
Permanent discontinuation due to headache	5.9%	0.9%	
Compliance (taking >75% of the time)	69.6%	76.8%	

Even if tolerance to headache occurs over time, risk of recurrent stroke is highest during the early period post stroke justifying the importance of full dose and good compliance. PRoFESS has produced results that do not favour ASA-ESDP over clopidogrel in the secondary prevention of stroke. Tolerance and compliance may be the chief determining factors if choosing between Clopidogrel and ASA-ESDP.

Glossary: CAPRIE *Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events* CHARISMA *Clopidogrel for High Atherothrombotic Risk and Ischaemic Stabilisation, Management and Avoidance* ESPRIT *European/Australasian Stroke Prevention in Reversible Ischaemia Trial* ESPS 2 *European Stroke Prevention Study 2* MATCH *Management of ATherothrombosis with Clopidogrel in High risk patients* PRoFESS *The Prevention Regimen for Effectively Avoiding Second Strokes*

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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