Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events: CHARISMA trial

The clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance (CHARISMA) trial was a prospective, multicentre, randomized, double-blind, placebo-controlled study to evaluate efficacy and safety of clopidogrel plus aspirin as compared with aspirin alone in patients at high risk for a cardiovascular event.

15 603 patients with either clinically evident cardiovascular disease or multiple risk factors were randomized to receive clopidogrel (75 mg per day) plus low dose aspirin (75 to 162 mg per day) or placebo plus low dose aspirin and followed them for a median of 28 months. The primary efficacy end point was a composite of myocardial infarction, stroke, or death from cardiovascular causes.

The rate of the primary efficacy end point was 6.8% with clopidogrel plus aspirin and 7.3% with placebo plus aspirin, and the difference was not statistically significant. The rate of severe bleeding was 1.7% and 1.3%. The rate of the primary end point among patients with multiple risk factors was higher with dual therapy compared to aspirin alone. In those with clinically evident atherothrombosis, the end point rate was lower with dual therapy than with aspirin alone.

Overall, clopidogrel plus aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiovascular causes for patients at high risk of atherothrombosis. New England Journal of Medicine 2006; 354: 1706-17.

The tendency to combine clopidogrel with aspirin for all patients at high risk of cardiovascular disease should be discouraged and clopidogrel should be given only for those who have an indication for additional antiplatelet therapy.

The effect of BCG vaccination on childhood tuberculous meningitis and military tuberculosis worldwide

BCG vaccine has shown consistently high efficacy against childhood tuberculous meningitis and miliary tuberculosis, but variable efficacy against adult pulmonary tuberculosis and other mycobacterial diseases. A meta-analysis assessed the costs and effects of BCG as an intervention against severe childhood tuberculosis in different regions of the world.

The study estimated that the 100.5 million BCG vaccinations given to infants in 2002 will have prevented 29,729 cases of tuberculous meningitis in children during their first 5 years of life, or one case for every 3435 vaccinations and 11,486 cases of miliary tuberculosis, or one case for every 9314 vaccinations.

The authors conclude that BCG vaccination is a highly cost-effective intervention against severe childhood tuberculosis and recommend that it should be retained in high incidence countries as a strategy to supplement the chemotherapy of active tuberculosis. Lancet 2006; 367: 1173-80.

Active and passive smoking and development of glucose intolerance: CARDIA study

The coronary artery risk development in young adults (CARDIA) study was done to assess whether active and passive smokers are more likely than non-smokers to develop clinically relevant glucose intolerance or diabetes. It was a prospective cohort study begun in 1985 with 15 years of follow up.

Men and women aged 18-30 years with no glucose intolerance at baseline, including current smokers, previous smokers, never smokers with reported exposure to secondhand smoke, and never smokers with no exposure to secondhand smoke were followed up. Time to development of glucose intolerance or taking antidiabetic drugs during 15 years of follow up was identified.

During follow up, 16.7% of participants developed glucose intolerance. A graded association existed between smoking exposure and the development of glucose intolerance. The 15-year incidence of glucose intolerance was highest among smokers (21.8%), followed by never smokers with passive smoke exposure (17.2%), and previous smokers (14.4%).

These findings support a role of both active and passive smoking in the development of glucose intolerance in young adulthood. British Medical Journal 2006; 332: 1064-9.

This study has identified another reason to avoid smoking in addition to the well known risks such as cardiovascular and cancer risk.

Suicide risk during antidepressant treatment

Population based data were used to evaluate the risk of suicide deaths in relation to initiation of antidepressant treatment, particularly to study whether there is an increased risk of suicide with newer antidepressants. Computerized health plan records were used to identify 65,103 patients with 82,285 episodes of antidepressant treatment between 1992 and 2003.
In the 6 months after the antidepressant treatment 31 suicide deaths (40 per 100 000 treatment episodes) and 76 serious suicide attempts (93 per 100 000) were identified in the study group. The risk of suicide attempt was 314 per 100 000 in children and adolescents compared to 78 per 100 000 in adults.

The risk of suicide was not significantly higher in the month after starting medication than in the subsequent months. Risk was highest in the month before starting treatment and declined progressively after starting medication. When the newer antidepressants were compared with older drugs an increase in risk after starting treatment was seen for older drugs.

Authors conclude that available data do not indicate a significant increase in risk of suicide with newer antidepressants. American Journal of Psychiatry 2006; 163: 41–7.

WHO analysis of causes of maternal deaths

WHO has done a systematic review including 35 197 maternal deaths to determine the distribution of causes of maternal deaths. Investigators recorded wide regional variation in the causes of maternal deaths. Haemorrhage was the leading cause of death in Africa (accounting for 33.9% with 4508 deaths) and in Asia (30.8%, 16 089 deaths). In Latin America and the Caribbean, hypertensive disorders were responsible for most deaths (25.7%, 11 777 deaths). Abortion deaths were the highest in Latin America and the Caribbean (12%), which can be as high as 30% of all deaths in some countries in that region. Deaths due to sepsis were higher in Africa, Asia and Latin America and the Caribbean than in developed countries.

The study concludes that haemorrhage and hypertensive disorders are major contributors to maternal deaths in developing countries. Evidence based reproductive health care policies and programmes should be provided at regional and national levels to reduce maternal deaths using these data. Lancet 2006; 367: 1066–74.

Risk modification of patients undergoing surgery

Administration of beta blockers and more recently statins have reduced the occurrence of perioperative ischaemic events. Now there is a shift in emphasis from risk stratification by non-invasive testing to risk modification by interventions which reduce perioperative ischaemia, principally beta blockade and treatment with statins. The recommendation is to identify patients at high risk of perioperative ischaemic events and use appropriate medical treatment such as beta blockers and statins to reduce risk. Heart 2006; 92: 17–20.

Self-poisoned patients in rural Sri Lanka

Self-poisoned patients admitted to Anuradhapura General Hospital and 17 surrounding peripheral hospitals were studied during a period of 6 months in 2002. A total of 742 patients were admitted to a secondary hospital and 81 died, a case fatality rate (CFR) of 10.9%; 483 patients were admitted to 17 surrounding peripheral hospitals, six patients (1.2%) died, 249 were discharged home and 228 were transferred to secondary hospitals. There was no effect of gender or age on likelihood of transfer, but patients who had ingested yellow oleander seeds or paraquat were more likely to be transferred than those who had taken organophosphates.

The authors conclude that 50% of patients admitted to peripheral hospitals were discharged home, showing that CFRs based on secondary hospital data are inflated. Although the incidence of self-poisoning is similar to that in England, fatal self-poisoning is three times more common in Sri Lanka than fatal self harm by all methods in England. Bulletin of the World Health Organisation 2006; 84: 276–82.

Diabetic heart disease

The existence of diabetic heart disease is now well recognized. It is defined as myocardial disease in patients with diabetes that cannot be attributed to hypertension, coronary artery disease or other known cardiac disease. Pathological, experimental and clinical evidence points towards the existence of diabetic cardiomyopathy which influences systolic and diastolic function, and is also correlated with impaired exercise capacity. The origin of the problem appears to be multifactorial. It is likely to contribute to adverse consequences of combined diabetes and heart failure. Further studies are expected to provide evidence for new treatment strategies for diabetic heart disease in the near future. Heart 2006; 92: 296–300.

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