ISCHAEMIC HEART DISEASE

Drug eluting stents and the treatment of in-stent restenosis ▶ With bare metal stents, restenosis can still occur in up to a third of cases. How can this be treated? After pre-treatment with 600 mg of clopidogrel for at least two hours before intervention, all patients were randomly assigned to one of three treatment groups: sirolimus stent, paclitaxel stent, or balloon angioplasty (100 patients in each group). The incidence of angiographic restenosis was 44.6% (41/92) in the balloon angioplasty group, 14.3% (13/91) in the sirolimus stent group (p < 0.001 vs balloon angioplasty), and 21.7% (20/92) in the paclitaxel stent group (p < 0.001 vs balloon angioplasty). The incidence of target vessel revascularisation was 33.0% (33/100) in the balloon angioplasty group, 8.0% (8/100) in the sirolimus stent group (p = 0.001 vs balloon angioplasty), and 19.0% (19/100) in the paclitaxel stent group (p = 0.02 vs balloon angioplasty). The secondary analysis showed a trend towards a lower rate of angiographic restenosis (p = 0.19) and a significantly lower rate of target vessel revascularisation (p = 0.02) among sirolimus stent patients compared with paclitaxel stent patients.


GIK does not benefit STEMI ▶ A meta-analysis suggested the benefit of glucose–insulin–potassium (GIK) infusions. This randomised controlled trial conducted in 20 201 patients with ST elevation myocardial infarction (STEMI) who presented within 12 hours of symptom onset were randomly assigned to receive GIK intravenous infusion for 24 hours plus usual care (n = 10 091) or to receive usual care alone (controls; n = 10 110). At 30 days, 976 control patients (9.7%) and 1004 GIK infusion patients (10.0%) died (hazard ratio (HR) 1.03, 95% confidence interval (CI) 0.95 to 1.13, p = 0.45). There were no significant differences in the rates of cardiac arrest, cardiogenic shock, or reinfarction. The rates of heart failure at seven days after randomisation were also similar between the two treatment groups. The lack of benefit of GIK infusion on mortality was consistent in prespecified subgroups, including those with and without diabetes, in those presenting with and without heart failure, in those presenting early and later after symptom onset, and in those receiving and not receiving reperfusion treatment (thrombolysis or primary percutaneous coronary intervention).


Aspirin plus PPI is better than clopidogrel alone for patients with GI upset ▶ Patients who took aspirin to prevent vascular diseases and who presented with ulcer bleeding were studied after the ulcers had healed and they were negative for Helicobacter pylori. Patients who took aspirin plus esomeprazole twice daily for 12 months. The end point was recurrent ulcer bleeding. The rate of recurrent ulcer bleeding was 2.7% (95% CI 1.8% to 3.6%) in the aspirin plus esomeprazole group and 4.4% (95% CI 3.1% to 5.9%) in the aspirin alone group (p = 0.001). This result was achieved by more than 50% reduction in both the number of ulcers and the number of persons with ulcers.


C Reactive protein and LDL values as joint targets for secondary prevention ▶ The PROVE-IT trial tested 80 mg of atorvastatin versus 40 mg of pravastatin in 3475 patients with acute coronary syndromes. Patients in whom statin treatment resulted in low density lipoprotein (LDL) cholesterol concentrations < 70 mg/dl (< 1.8 mmol/l) had lower event rates than those with higher concentrations (2.7 v 4.0 events per 100 person-years, p = 0.008). Concentrations of C reactive protein (CRP) and of LDL did not appear to be related. However, a significant difference was observed between those who had CRP concentrations < 2 mg/l after statin treatment and those who had higher values (2.8 v 3.9 events per 100 person-years, p = 0.006). This effect of raised CRP was present at a similar magnitude at all values of LDL cholesterol achieved. Although atorvastatin was more likely than pravastatin to result in low concentrations of LDL cholesterol and CRP, meeting these targets was more important in determining the outcomes than was the specific choice of treatment. Patients who had LDL cholesterol concentrations < 1.8 mmol/l and CRP concentrations < 1 mg/l after statin treatment had the lowest rate of recurrent events (1.9 per 100 person-years). In addition, in the REVERSAL study, patients with reductions in both LDL cholesterol and CRP that were greater than the median had significantly lower rates of progression of plaque on intravascular ultrasound than patients with reductions in both biomarkers that were less than the median (p = 0.001). Thus both event rate reduction and plaque burden reduction appear to be linked to CRP reduction, as well as LDL reduction.


GENERAL CARDIOLOGY

Is warfarin needed for atrial flutter? ▶ In atrial fibrillation (AF), cardiovascular without anticoagulation carries a 5% risk of thromboembolism, while anticoagulation reduces risk of stroke by 60–70% long term. For atrial flutter, this review finds that there are 13 studies of the risk of cardioversion, and four of long term risk. Event rates for cardioversion varied from 0–7.3%, based on prior risk (that is, previous thromboembolism, no screening by echocardiography, no prior use of anticoagulants). It proved impossible to estimate the effect of aspirin treatment. Long term risk of embolic events appears to be about 3% per year without anticoagulation. In a long term study of Medicare patients, one third of flutter patients developed AF, and the risk of thromboembolism was increased compared to patients without AF or atrial flutter. Conclusion—it is probably worth anticoagulating flutter.


Diastolic dysfunction is a rare cause of dyspnoea in the elderly ▶ A total of 152 subjects with dyspnoea underwent echocardiography, electrocardiography, and lung function testing. Subjects with normal lung function test results (n = 60) underwent cardiac magnetic resonance imaging, chest radiography, exercise tests, and blood tests. Left ventricular diastolic dysfunction was assessed by a variety of echocardiographic/Doppler techniques. Of 129 subjects with dyspnoea, 81 (63%) had signs of lung disease or “obvious” cardiac disease. In the remaining 48 subjects, 32 (67%)...
had a potential cardiac/non-cardiac cause of dyspnoea. In all subjects with dyspnoea, 1–11% had diastolic dysfunction, and in the 48 remaining subjects, 0–10% had isolated diastolic dysfunction, depending on the definition used.

Implantable defibrillators offer more survival benefit than amiodarone in patients with impaired LV function and CHF ▶ A total of 2521 patients with New York Heart Association (NYHA) class II or III congestive heart failure (CHF) and a left ventricular ejection fraction (LVEF) of 35% or less were assigned to conventional treatment for CHF plus placebo (847 patients), conventional treatment plus amiodarone (845 patients), or conventional treatment plus a conservatively programmed, shock-only, single lead implantable cardioverter-defibrillator (ICD) (829 patients). Placebo and amiodarone were administered in a double blind fashion. The median LVEF in patients was 25%; 70% were in NYHA class II, and 30% were in class III CHF. The cause of CHF was ischaemic in 52% of patients and non-ischaemic in 48%. The median follow up was 45.5 months. There were 244 deaths (29%) in the placebo group, 240 (28%) in the amiodarone group, and 182 (22%) in the ICD group. As compared with placebo, amiodarone was associated with a similar risk of death (HR 1.06, 97.5% CI 0.86 to 1.30; p = 0.53), and ICD therapy was associated with a decreased risk of death of 23% (HR 0.77, 97.5% CI 0.62 to 0.96; p = 0.007) and an absolute decrease in mortality of 7.2 percentage points after five years in the overall population. There was a rate of appropriate shocks in the ICD group of 5% per year. Of note is that this was single chamber ICD implantation. A trial of dual chamber ICDs failed to show benefit (AMIOVIRT study) previously. In fact, there is a trend towards biventricular ICD implantation in patients with heart failure. Data for this approach are emerging.

Ximelagatran for AF ▶ In a double blind, randomised, multicentre trial (2000–2001) 3922 patients with non-valvar AF and additional stroke risk factors were randomised to ximelagatran or warfarin (international normalised ratio (INR) 2–3). The mean (SD) INR with warfarin of 2.4 (0.8) was within target during 68% of the treatment period. The stroke event rate with ximelagatran was 1.6% per year and with warfarin was 1.2% per year (absolute difference 0.45% per year, 95% CI –0.13% to 1.03% per year; p < 0.001 for the predefined non-inferiority hypothesis). When all cause mortality was included in addition to stroke and systemic embolic events, the rate difference was 0.10% per year (95% CI –0.97% to 1.2% per year; p = 0.86). There was no difference between treatment groups in rates of major bleeding, but total bleeding (major and minor) was lower with ximelagatran (37% v 47% per year, 95% CI for the difference –14% to –6.0% per year; p < 0.001). Serum alanine aminotransferase concentrations rose to greater than three times the upper limit of normal in 6.0% of patients treated with ximelagatran, usually within six months, and typically declined whether or not treatment continued; however, one case of documented fatal liver disease and one other suggestive case occurred. This may limit generalised availability of this drug.

Journals scanned

Reviewers
Dr Diana Gorog, Dr Akhil Kapur, Dr Masood Khan, Dr Alistair Lindsay, Dr Andrew Sharp

FROM BMJ JOURNALS

Lipid lowering drugs prescription and the risk of peripheral neuropathy: an exploratory case-control study using automated databases

G Corrao, A Zambon, L Bertu', E Botteri, O Leoni, P Contiero

Study objective: Although lipid lowering drugs are effective in preventing morbidity and mortality from cardiovascular events, the extent of their adverse effects is not clear. This study explored the association between prescription of lipid lowering drugs and the risk of peripheral neuropathy.

Design: A population based case-control study was carried out by linkage of several automated databases.

Setting: Resident population of a northern Italian Province aged 40 years or more.

Participants: Cases were patients discharged for peripheral neuropathy in 1998–1999. For each case up to 20 controls were randomly selected among those eligible. Altogether 2040 case patients and 36 041 controls were included in the study.

Exposure assessment: Prescription drug database was used to assess exposure to lipid lowering drugs at any time in the one year period preceding the index date.

Analysis: Conditional logistic regression model for matched data was used to estimate the risk of peripheral neuropathy associated with exposure to statins, fibrates, and other lipid lowering drugs.

Main results: Weak but significant effects of lipid lowering drugs as a whole (matched odds ratio: 1.27; 95% confidence intervals 1.05 to 1.55), statins (1.19; 1.00 to 1.40), and fibrates (1.49; 1.03 to 2.17) were observed. Significant linear trends towards increased risk at increased exposure to both statins and fibrates were observed.

Conclusions: The use of both statins and fibrates was associated with the risk of peripheral neuropathy. The primary purpose of this exploratory study is signal generation. This requires further investigations to evaluate the causal role of lipid lowering drugs on the onset of peripheral neuropathy.

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