



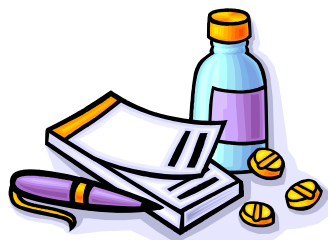
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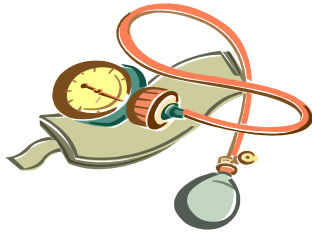
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Does Ezetimibe ENHANCE survival? Ezetimibe, a cholesterol-absorption inhibitor, has been shown to reduce low-density lipoprotein cholesterol (LDL-C) when added to statin treatment. However, its effect on the progression of atherosclerosis remains unknown. A recent randomised double-blind study compared the effects of simvastatin 80mg, with/without ezetimibe 10mg daily X 2 years, on the progression of atherosclerosis in 720 patients with familial hypercholesterolaemia (ENHANCE study, *NEJM 2008; 358: 1431-43*). Patients had ultrasonography of the carotid and femoral arteries, to evaluate mean intima-media thickness (a surrogate marker for atherosclerosis) at baseline and repeated after 24 months' treatment. Approximately 80% of patients in each group had previously received statin therapy. Results showed that the combination group achieved significantly lower levels of LDL-C (mean levels of 3.65mmol/L down from 8.25 at baseline) compared with the monotherapy group (mean levels of 4.98mmol/L down from 8.22 at baseline). Combination therapy also produced a significant reduction in the level of triglycerides and C-reaction protein (6.6% and 25.7% respectively) compared with monotherapy. Percentage increases of 7.8% for monotherapy and 10.2% for combination therapy were noted for HDL-C (p=0.05). **However, there was no significant difference in intima-media thickness between the groups.** The authors note that the greater reductions in LDL-C and C-reactive protein in the combination group did not translate into an improvement in terms of intima-media thickness. They postulate that this may be due to the fact that certain lipid-independent effects of statins, not shared by ezetimibe might be involved in the production of a vascular benefit. The findings might also be due to the fact that the majority of these familial hypercholesterolaemia patients had previous statin treatment, which might have depleted plaque lipids resulting in plaque stability and clinical quiescence. An accompanying editorial (*NEJM 2008; 358: 1504-7*) notes that the intima-media thickness is considered to be a valid surrogate marker for atherosclerosis, but that a 2-year study might be too short to note a difference between the groups in terms of vascular protection. The author outlines the recently issued recommendations from the American College of Cardiology: first achieve target for levels of LDL-C and HDL-C (or of the ratio of total cholesterol to HDL-C) with use of statins plus drugs that have shown clinical benefits when added to statins (e.g. nicotinic acid, fibrates, bile acid sequestrants) as tolerated: use ezetimibe in patients who, despite these therapies do not achieve their individual targets. [Editor's note: Ezetimibe is also authorised as monotherapy in patients in whom a statin is considered inappropriate or is not tolerated. Check out the NICE appraisal of ezetimibe in primary hypercholesterolaemia (TA132, Nov 2007) for more background information. www.nice.org.uk].

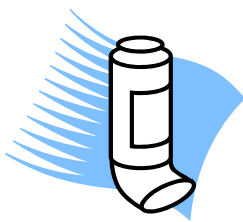


Statins can reduce your blood pressure! A recent study looked at the effects of statin therapy on patients' blood pressure (BP) (*Arch Intern Med 2008; 168 (7):721-727*). This study was part of a larger trial (randomised statin study comparing simvastatin, pravastatin with placebo over 6 months). A total of 973 patients with known baseline BP measurements, no known cardiovascular disease or diabetes mellitus and LDL cholesterol levels of 3.0mmol/l - 4.9mmol/l were included in this study. BP was measured and results in statin-treated patients compared with those on placebo. **Overall results showed significant, though modest BP reductions in the combined statin group compared with placebo at 6 months** (= systolic BP drop of 2.2mmHg (p=0.02) and diastolic BP drop of 2.4mmHg (p<0.001)). Reductions were noted in patients without hypertension - i.e. who had neither high BP at baseline nor were receiving BP medication - and findings were stronger when patients with high BP at baseline were excluded. The effects on BP had dissipated 2 months after discontinuation of statin treatment. The authors concluded that statins lower both systolic and diastolic BP relative to placebo and the effects extend to normotensive patients even though the change was modest. **They suggest that these modest effects on BP may contribute to the reduced risk of stroke and cardiovascular events reported on statins.**



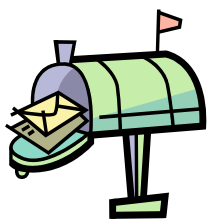
Treating high blood pressure is beneficial in patients aged 80 years and older.

Elevated blood pressure (BP) is common in persons aged 80 years and over, a group that constitutes the fastest-growing segment of the general population in developed countries. Although BP reduction is known to be effective in lowering cardiovascular disease risk, including stroke, in the general population, there are mixed results relating to those aged ≥ 80 years. A recent randomised controlled double-blind study compared the effectiveness of the diuretic indapamide (1.5mg sustained release) +/- perindopril (2mg or 4mg) with matching placebos in 3,845 patients aged ≥ 80 years, with sustained systolic BP > 160 mmHg (*NEJM* 2008; 358: 1887-98). The target BP was 150/80mmHg. Follow up was for a median of 1.8 years. Results showed a mean BP drop of 15.0/9.1mmHg in the treated groups compared with placebo. For the primary endpoint (fatal or non fatal stroke) there were 51 events in the treated groups compared with 69 events on placebo. This equates to a significant 30% reduction in events. In addition, there was a significant reduction in death from any cause and in the rate of heart failure. The beneficial effects were noted from one year and treatment was not associated with serious adverse events. The authors conclude that this large study provides unique evidence that reduction of BP, based on this combination of treatment is beneficial. [Editor's note: perindopril has been re-formulated and is now available in 5mg and 10mg strengths. The lower dose used in this study is not authorised in Ireland]



Commercial versus home-made "spacers" for bronchodilator therapy in children

A recent Cochrane review compared the response to inhaled beta-2 agonists delivered through metered-dose inhaler attached to home-made spacers with commercially produced spacers in children with acute exacerbations of wheezing or asthma (*Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD005536. DOI: 10.1002/14651858.CD005536.pub2). Six randomised controlled trials (n = 658) were included in the meta-analysis, all of which were relatively small, conducted mainly in developing countries and using either plastic drink bottles or cardboard cones as home-made spacers to valved commercial spacers. The primary outcome measure was the need for hospital admission, with secondary outcomes including: changes from baseline in PEFr, FEV₁ and oxygen saturation (SaO₂). The review did not identify a significant difference in the two delivery methods in terms of hospital admission, change in SaO₂, clinical score, change in PEFr and need for additional treatment. The authors however consider that the results of this review should be interpreted with caution in view of a number of factors including: the small number of RCTs meeting the criteria for inclusion, absence of the primary outcome of interest and other clinically important outcomes in the majority of included studies. They recommend that in selecting a spacer device for an individual patient, a commercial spacer should be used with home-made spacers only being used if commercial devices are not available. They conclude that further studies are required before confident conclusions can be drawn about the efficacy of home-made spacers in children [Editor's note: don't forget that the Cochrane library is available free of charge in Ireland at www.hrb.ie - click on the Cochrane logo]



*****Reminder** The NMIC needs you.*** We wish to thank all those GPs who returned the questionnaire sent with the last NMIC mailing, seeking comments on the NMIC bulletins and Newsletters. This feedback is very helpful and will be used to improve our publications in the future. The response rate has been good so far, however we wish to receive as many responses as possible by 30th May. If you have mislaid your questionnaire and would like to send feedback, just e-mail

nmic@stjames.ie and we will send you out another one. Results will be published on our website (www.nmic.ie). We look forward to your comments!