POEMs

Patient-Oriented Evidence that Matters

The POEMs selected for June are a rather negative lot. They inform us that there is no best evidence for the treatment of bronchiolitis, that lowering homocysteine levels does not prevent recurrent stroke and that routine screening of heart disease in low risk adults using ECGs, ETTs or CT is not recommended. None of these may affect your current practice but it is interesting that there is little evidence for some commonly held beliefs. On a more positive note there is evidence that strontium ranelate is a useful alternative for post-menopausal women who have had a previous vertebral fracture. Editor.

Clinical Question

How effective are the various treatments for bronchiolitis?

Bottom Line

In spite of the large number of studies assessing various treatments for bronchiolitis, in general the studies have been small, of poor quality, and don't assess clinically important end points. The treatments may be effective, however, just unproven. To really judge their effectiveness, we'd need large, well-designed studies that include clinically important outcomes. Until then, bronchiolitis treatment is in the 'can do, but not required' category – there are few 'musts' or 'must nots,' so don't obsess about overtreatment or undertreatment. (LOE = 1a–)

Reference

King VJ, Viswanathan M, Bordley WC, et al. Pharmacologic treatment of bronchiolitis in infants and children: a systematic review. Arch Pediatr Adolesc Med 2004; 158:127-37.

Study Design

Systematic review

Setting

Various (meta-analysis)

Synopsis

The authors systematically reviewed Medline and the Cochrane Collaboration Database of Controlled Clinical Trials for randomised controlled trials published in English that assessed the effectiveness of various treatments for bronchiolitis. They used an explicit and reasonable set of search terms and did a limited search for unpublished data. The team assessed the quality of each study with disagreements adjudicated by consultation and consensus. The authors reported on 44 studies of the most commonly used agents: epinephrine, beta2-agonist bronchodilators (albuterol and salbutamol), corticosteroids, and ribavirin. They found a handful of studies evaluating inhaled helium, RSV-immunoglobulin, Chinese herbs, and so forth, but chose not to report these data in the paper. If interested, these are reported in an AHRQ Evidence Report at www.ahrq.gov/clinic/evrptfiles.htm#bronch. In general, most studies were quite small, of limited quality, looked at short-term improvement, and failed to assess clinically important outcomes. Racemic epinephrine was studied against beta2-agonists in eight randomised controlled trials of 660 infants. Five of these studies assessed hospitalisation, only two reported either fewer admissions or shorter stays. Most of the 13 studies of nebulised beta2-agonists had multiple treatment arms: saline placebos, unspecified placebos, ipratropium, oral agents, for example. Seven of the studies assessed hospitalisation, none reported meaningful differences in rate or duration. Four studies evaluated oral corticosteroids and found no consistent effect on hospitalisations or duration of stay. Parenteral corticosteroids had no effect on clinical outcomes. In 10 randomised controlled trials of ribavirin (Copegus, Rebetol), the overall study quality was low. Of the five studies reporting on clinically important outcomes, four failed to demonstrate any effect on rate of hospitalisation, length of stay, duration of illness, or use of intensive treatment. The sole study finding a benefit (on use of intensive treatment) used sterile water as the placebo. But since sterile water can induce bronchospasm, thereby making ribavirin appear more effective, this study has been criticised.

** Patient-Oriented Evidence that Matters. See editorial (NZFP 2003; 30:150)*

Clinical Question

Does lowering the homocysteine level in patients with ischemic stroke prevent recurrent stroke?

Bottom Line

Lowering homocysteine levels with a high dose B-vitamins in patients with ischemic stroke did not lower the risk of recurrent stroke. This study had the ability to detect a 30% difference in stroke rates over two years, if one exists. The likelihood of dying or experiencing a myocardial infarction was not affected by the therapy, although the study was probably too small and too short to find a difference if one truly exists. It seems benign (and possibly helpful) to recommend a multivitamin supplement for all patients at risk of atheroschlerotic vascular disease. There does not, however, appear to be any solid evidence yet supporting routine measurement of homocysteine levels. (LOE = 1b)

Reference

Toole JF, Malinow MR, Chambless LE, et al. Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death. The Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. JAMA 2004; 291:565-75.

Study Design

Randomised controlled trial (double-blinded)

Setting

Inpatient (any location) with outpatient follow-up

Synopsis

Observational studies have suggested that elevated homocysteine levels are associated with an increased risk of recurrent stroke, acute coronary events, and mortality. Folic acid supplements have been suggested as a means to lower homocysteine levels and reduce these risks. Fifty-six centres in the United States, Canada, and Scotland coordinated to enrol 3680 adults with nondisabling cerebral infarction. The patients received the best medical and surgical care and were randomised in double-blind fashion (concealed allocation assignment) to receive an identical daily supplement of either a high-dose multivitamin (pyridoxine 25mg, cobalamin 0.4mg, and folic acid 2.5mg) or low-dose multivitamin (pyridoxine 200mcg, cobalamin 6mcg, and folic acid 20mcg) preparation. Participants were contacted every three months by telephone or clinic visits for up to two years. A total of 93% of subjects were available for follow-up analysis. Although the article does not specify that outcomes were assessed by individuals blinded to treatment group assignment, contact with the corresponding author confirmed that this was true. Using intention-to-treat analysis, the mean reduction in total homocysteine level was significantly greater in the high-dose group, but there were no significant differences between the two treatment groups regarding recurrent stroke, acute coronary event, or death. The study had an 80% power to detect a 30% reduction in recurrent ischemic stroke over two years of follow-up.

Clinical Question

Should high-tech means of screening be used to identify heart disease in asymptomatic individuals?

Bottom Line

The United States Preventive Services Task Force recommends against routine screening of adults at low risk of heart disease using electrocardiography (ECG), exercise treadmill testing, or computerised tomography (CT) because the harms of screening (additional testing of patients with a false-positive result, labelling of patients with a disease) outweigh the benefits. There is insufficient evidence to support this type of testing even in patients at increased risk. (LOE = 2b)

Reference

US Preventive Services Task Force. Screening for coronary heart disease: Recommendation statement. Ann Intern Med 2004;140.

Study Design

Practice guideline

Setting

Various (guideline)

Synopsis

Can screening for disease be harmful, even if the test itself is benign? There are actually many risks associated with screening for disease, which is a hard concept for many patients to grasp, since, after all, if even only one person is found to have the disease, isn't it 'worth it'? The problem with screening occurs not with the people who truly have the disease (of course) but with patients who have a positive test result even though

they don't really have the disease (i.e., false positive results). These patients frequently undergo further testing to rule out the disease, may receive unnecessary treatment, and may be labelled as having a disease that they don't have, with all its attendant psychological and financial (i.e., life insurance) issues. There is also a risk of inappropriate reassurance of patients who have the disease but it's not detected by the screening test (i.e., false negative results). So is the case with screening for heart disease. The screening tests often used – a baseline ECG, treadmill testing, or CT, are fairly poor at distinguishing patients with heart disease from those who don't. In asymptomatic people, ECG changes are present in less than 10% of patients with heart disease. The positive predictive value of exercise stress testing ranges from 6% – 48%, meaning that up to 94% of patients with a positive stress test are not at risk for a cardiovascular event. There are no data evaluating CT testing in asymptomatic patients. From this information the Task Force concluded that the risks outweigh the benefits in asymptomatic patients. The tests do better in patients at high risk, but there is still significant risk of false-positive results. The Task Force concluded there is insufficient data to support the use of screening in these patients. They suggest relying on the various clinical prediction rules available to estimate heart disease risk, and base management decisions on the results from these rules.

Clinical Question

Does strontium ranelate improve clinical outcomes in patients with postmenopausal osteoporosis and at least one previous vertebral fracture?

Bottom Line

Strontium ranelate prevents one symptomatic vertebral fracture for every 17 postmenopausal women with a history of vertebral fracture who take it for three years. (LOE = 1b)

Reference

Meunier PJ, Roux C, Seeman E, et al. The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. N Engl J Med 2004; 350:459-68.

Study Design

Randomised controlled trial (double-blinded)

Setting

Outpatient (any)

Synopsis

Strontium ranelate is thought to both increase the formation of new bone and decrease bone resorption. In this study, postmenopausal women with osteoporosis and at least one previous vertebral compression fracture were randomly assigned (allocation concealment uncertain) to 2 grams strontium powder per day or placebo. The powder could be taken once or twice daily, and follow-up consisted of annual radiographs and patient report of any acute back pain or fracture. Although 1649 patients were initially recruited, 198 were excluded from the analysis because they had no follow-up radiographs, leaving 1442 (719 receiving strontium, 723 receiving placebo) for the intention-to-treat analysis. The mean age of patients was 69 years, with a body mass index of 26.1, and a mean of 2.2 previous vertebral fractures. A total of 1260 completed the planned three-year follow-up. The study was funded by the manufacturer, the French pharmaceutical company Servier, who held the data and conducted all of the statistical analyses for the authors. After three years, the risk of symptomatic vertebral fracture, the more important patient-oriented outcome, was lower in the treatment group (11.3% vs 17.4%; $P < .001$; absolute risk reduction [ARR] = 6.1%; number needed to treat [NNT] = 17). There was also a significant reduction in the risk of radiographic vertebral fractures in the strontium group; that is, fractures noted on film but not necessarily apparent to the patient (20.9 vs 32.8%; $P < .001$; ARR = 10.9%; NNT = 9). There was no significant difference in the risk of nonvertebral fracture (15.6% vs 16.9%) and a nonsignificant trend toward fewer episodes of back pain in the strontium group (17.7% vs 21.3%; $P = .07$). Bone mineral density increased in the spine, hip, and femoral neck in the strontium group compared with no change or a small decline in the placebo group. Adverse events were generally similar between groups, with slightly more diarrhoea in the strontium group (6.1% vs 3.6%; $P = .02$).