POEMs

Patient-Oriented Evidence that Matters

The first of our POEMs for April adds to our options for the management of patients who have acute low back pain. It provides us with evidence-based guidelines about those patients who will most likely benefit from spinal manipulation. Our second and third POEMs respectively caution against the early use of calcium channel blockers in the management of hypertension and the use of vitamin E supplementation in any patients. Finally, a meta-analysis reveals that we should have known about the cardiovascular risks of rofecoxib five years ago! Editor.

Clinical question

Can a simple rule be used to predict which patients with low back pain will receive benefit from spinal manipulation?

Bottom line

A clinical decision rule can be used to determine which patients with low back pain will receive benefit from a series of two spinal manipulation sessions given over one week. As compared with exercise treatment, the number needed to treat with spinal manipulation is two if the rule is positive. The rule gives one point for an affirmative answer to each question, and scores of four or five (out of five) predict response to spinal manipulation. The five questions are: (1) Is the duration of the pain less than 16 days? (2) Is there no pain below the knee? (3) Is this patient's fear-avoidance beliefs questionnaire score less than 19? (4) Is there at least one hypomobile segment in the lumbar spine? And, (5) Is there at least one hip with greater than 35 degrees of internal rotation range of motion? (LOE=1b)

Reference

Childs JD, Fritz JM, Flynn TW, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. Ann Intern Med 2004; 141:920-28.

Study Design

Decision rule (validation)

Allocation

Concealed

Setting

Outpatient (specialty)

Synopsis

This study was designed to validate a previously developed clinical decision rule to determine which patients with low back pain will benefit from spinal manipulation therapy. The high-velocity thrust manipulation therapy used in the study was not provided by a chiropractor or an osteopath, but by a physical therapist. The investigators enrolled 131 consecutive patients who were referred for physical therapy for the treatment of low back pain. Patients were an average age of 34 years and 40% were women. The clinical decision rule (see Bottom-line) was applied to all patients but was not used to determine therapy. Instead, after the rule was calculated, half the patients were assigned to receive manipulation therapy and range-of-motion exercises for two sessions during the first week, followed by a low-stress aerobic and lumbar spine strengthening programme weekly for another three weeks. The control group received the same frequency of treatment, but the treatment was limited to the strengthening programme. Both groups were instructed to stay active. The test of cure of the low back pain was an improvement on the Owestry Disability Questionnaire of at least 50% from baseline. Using the rule, 47 of the 131 patients (36%) would have been referred for manipulation, and these patients were evenly distributed between the two treatment groups. After one week (two sessions), 44.3% of the patients receiving manipulation achieved success as compared with 11.5% of the control group patients (number needed to treat [NNT]=3; 95% CI, 2.2–5.7). After four weeks, 62.9% vs 36.1% of patients met the criteria for success (NNT=4; 2.4–10.4). In evaluating the rule, a positive result on the rule resulted in a likelihood ratio of 13.2 (3.4–52.1). If the rule had been used to select patients who likely would respond to manipulation therapy, the number needed to treat would have been 1.3 (1.1 1.9) at one week and 1.9 (1.4–3.5) at four weeks.

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

Clinical question

In the treatment of adults with hypertension, which other drug class added to diuretics most effectively reduces adverse cardiovascular events?

Bottom line

In women with hypertension and no history of cardiovascular disease (CVD), a regimen of a diuretic plus either a B-blocker or angiotensin-converting enzyme (ACE) inhibitor reduces the risk of CVD mortality compared with a diuretic plus calcium channel blocker. The evidence continues to mount that calcium channel blockers should be the agent of last resort in the treatment of most patients with hypertension. (LOE=2b-)

Reference

Wassertheil-Smoller S, Psaty B, Greenland P, et al. Association between cardiovascular outcomes and antihypertensive drug treatment in older women. JAMA 2004; 292:2849-59.

Study Design

Cohort (prospective)

Setting

Population-based

Synopsis

Evidence shows that diuretics are equal to or superior to other agents as first-line therapy for most patients with hypertension. More than one drug class, however, is frequently required to control hypertension. It is unclear which other drug classes, added to diuretics, optimally reduce adverse cardiovascular events. The investigators evaluated data obtained from women with hypertension enrolled in the Women's Health Initiative Observational Study, a prospective cohort study of 93 676 women aged 50 to 79 years at baseline. Of these, 94% were followed up for a mean of 5.9 years. Antihypertensive medication was determined from original bottles brought to baseline visits and matched to a pharmacy database. End points were ascertained from mailed questionnaires, direct report, telephone follow-up, medical records, and death certificates. The investigators do not specifically state whether outcomes were assessed by individuals blinded to treatment groups. Among women with hypertension but no history of CVD, monotherapy with calcium channel blockers versus diuretics was associated with an increased risk of CVD death (number needed to treat to harm over six years [NNTH/6]=143; 95% CI 59–3898). In similar patients, a two-drug regimen of a diuretic plus calcium channel blocker was associated with a statistically significant increase in CVD death compared with both a diuretic plus beta-blocker and a diuretic plus ACE inhibitor (NNTH/6 years = 93; 34–3898). Both analyses were adjusted for age, race/ethnicity, smoking, high cholesterol requiring medication, body mass index, physical activity, hormone use, and diabetes.

Clinical question

In patients with or without heart disease, does vitamin E supplementation decrease mortality?

Bottom line

Vitamin E supplementation does not decrease all-cause mortality in patients with or without pre-existing heart disease. At higher doses it can actually be harmful, although the deleterious effect is small (number needed to treat to harm = 250). (LOE=1b)

Reference

Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med 2005; 142:37-46.

Study Design

Meta-analysis (randomized controlled trials)

Setting

Outpatient (any)

Synopsis

The antioxidant property of vitamin E has led many to use it to prevent cardiovascular or cancer-related mortality. However, several studies and several previous meta-analyses have shown either no benefit or a slight increase in mortality with its use. The authors of this study performed

a literature search in the usual way, searching MEDLINE, the Cochrane Clinical Trials Database, and reference lists and files. They included 19 randomised studies of almost 136 000 patients comparing vitamin E with a control or placebo group for at least one year and with at least 10 deaths in the trial. Study subjects varied and included elderly patients, healthy adults, and patient with cardiovascular disease. Study results were analysed by intention to treat. The method of data extraction was not explained and studies were not graded or selected on the basis of quality. In the studies the baseline death rate was approximately 10%. Overall, there was no difference in all-cause mortality between the control group and placebo group. However, when comparing low-dose versus high-dose vitamin E (less than 400IU/day vs 400IU/day or more), differences were found. In the studies of lower doses, there was no benefit or detriment to vitamin E supplementation (relative risk = 0.98; 95% CI, 0.96–1.01). When high dose supplementation was studied separately, the risk was slightly but significantly higher in the supplemented group, with a number needed to treat to harm of 250 (143–998). The effect of vitamin E supplementation was not different when the results were evaluated by patient's sex or average age, or by the length of follow-up.

Clinical question

When were the risks of rofecoxib (Vioxx) well established?

Bottom line

If anyone had been minding the store and looking at the cumulative data as they became available, rofecoxib would have been associated with an increased cardiovascular risk by the end of 2000. United States government agencies and other watchdogs failed to recognise the risk. Clinicians need to be wary about the selective reporting of harms and benefits of new drugs. (LOE=1a)

Reference

Juni P, Nartey L, Reichenbach S, et al. Risk of cardiovascular events and rofecoxib: cumulative meta-analysis. Lancet 2004; 364:2021-9.

Study Design

Meta-analysis (other)

Setting

Various (meta-analysis)

Synopsis

Rofecoxib (Vioxx) was removed from the market under a hailstorm of controversy. The manufacturer apparently decided to remove it on the basis of a single small trial. Among the controversial issues was whether the manufacturer covered up known harms and manipulated the release of data to provide a favourable outlook, and whether the manufacturer inappropriately created demand by skewing the information reported to the public. These authors searched the Cochrane Controlled Trials Register and several other databases (including MEDLINE, EMBASE, and CINAHL), examined citations of key papers in the Science Citation Index, searched conference proceedings, screened reference lists of relevant papers, contacted experts, and reviewed the proceedings of the Food and Drug Administration advisory panels. They were in search of all randomised clinical trials comparing rofecoxib with another anti-inflammatory drug or placebo. Since they found no large-scale comparisons with other drugs, they also identified observational studies. Two people independently extracted the data using an explicit approach. Two other researchers independently checked the data. The researchers evaluated two key quality issues in the clinical trials: concealed allocation and independent external review of serious adverse events. Finally, they analysed the study data using standard meta-analytic methods (also on a cumulative basis). For this latter evaluation, they included cardiovascular safety data in the year they first became available. The authors found 18 placebo-controlled trials (including more than 25 000 patients; all trials sponsored by the manufacturer) and 11 observational studies. If all the data had been evaluated systematically on an ongoing basis, the cumulative risk of acute myocardial infarction would have become significant by the end of 2000.
