POEMs

Patient-Oriented Evidence that Matters

For August we have only selected POEMs with high quality (level 1) evidence. First we have evidence that low-dose long-term warfarin is a safer alternative (to placebo or conventional warfarin treatment) following an 'idiopathic' DVT. The next POEM informs us that hypertension management is the single most important aspect of treatment for patients who have type 2 diabetes and that using thiazides is OK. Our third POEM is food for thought. What does it mean when we learn that women who have a false-positive mammogram are more likely to return for follow-up screening? Finally there is some evidence that runs counter to my usual practice when advising women about taking COCs. This study appears to be telling us that taking COCs continuously (leaving out the 'sugar' pills) is actually OK – Editor

Clinical question

Is low-dose warfarin a reasonable option for long-term anticoagulation?

Setting

Outpatient (any)

Study design

Randomised controlled trial (double-blinded)

Synopsis

Therapy of acute deep vein thrombosis (DVT) involves anticoagulation to a target international normalised ratio (INR) of 2.0 to 3.0. Patients with recurrent thromboemboli after anticoagulation is discontinued are increasingly being placed on long-term anticoagulation with warfarin. However, this is associated with a significant risk of major bleeding complications: 4% to 9% per year. Perhaps a lower intensity of anticoagulation would provide most of the benefit, with less risk of bleeding? This study included patients older than 30 years with an idiopathic DVT (that is, not associated with surgery or trauma); excluded were those with metastatic malignancy, a history of major gastrointestinal bleeding or stroke, a life expectancy of less than three years, or who were taking an antiplatelet agent other than 325mg aspirin per day. Patients (n=578) first had to complete a 28-day run-in period to evaluate their compliance and ease of anticoagulation. Only those who were at least 85% compliant and whose INR could be maintained in the range between 1.5 and 2.0 without exceeding a dose of 10mg warfarin per day were included in the study (n=508). Randomisation to warfarin (target INR=1.5–2.0) or placebo was done centrally to conceal allocation, and considerable efforts were made to blind both patients and physicians to treatment assignment. For example, the device used to measure the INR gave a fake INR to the physician for a placebo patient but sent the real value back to the study centre. The dose was adjusted using a standard algorithm, with office visits every two months.

Groups were similar at baseline and analysis was by intention to treat. The primary outcome was an 'all bad things' composite of recurrent DVT, pulmonary embolism, haemorrhage requiring transfusion or hospitalisation, haemorrhagic stroke, or death. The study was stopped early once the benefit tipped in favour of the warfarin group, after a mean follow-up of 2.1 years. The median INR of patients in the treatment group was 1.7, compared with 1.0 for those in the placebo group. Patients taking warfarin had fewer episodes of recurrent venous thromboembolism (2.6 vs 7.2 per 100 person-years; P<.001; number needed to treat [NNT]=22 for one year). There was no significant difference in the risk of death, cancer, or myocardial infarction, and there were more minor bleeding episodes in the warfarin group (12.8 vs 6.7 per 100 person years; P=.002, number needed to harm [NNH]=16.4 for one year). There were two major haemorrhages in the placebo group and five in the warfarin group, but this difference was not statistically significant. The composite outcome favoured the warfarin group, as well (4.1 vs 8.0 events per 100 person years; P=0.01; NNT=26 for one year). The benefit was consistent in a variety of subgroup analyses.

Bottom line

For every 26 persons who take warfarin targeted to an INR of 1.5 to 2.0 for one year, one bad outcome is pre-

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

vented. This is a lower-risk option than traditional warfarin dosing to a target range of 2.0 to 3.0; note that treatment of a DVT or PE to an INR of 2.0 to 3.0 for the initial three to 12 months is still recommended.

Level of evidence

(http://www.infopoems.com/levelsofevidence.cfm)
1b

Reviewed by

ME

Reference

Ridker PM, Goldhaber SZ, Danielson E, et al. Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. N Engl J Med 2003; 348:1425–34.

Clinical question

What is the role of blood pressure control in patients with type 2 diabetes?

Setting

Various (guideline)

Study design

Practice guideline

Synopsis

Aggressive control of blood pressure, with a goal of achieving <135/<80 mmHg, is the single most important management aspect for patients with type 2 diabetes. Unlike aggressive blood glucose control, blood pressure control has been shown to decrease clinically relevant macrovascular and microvascular events that occur with diabetes, as well as prolong life. From the report: *'We do not intend to suggest that glycemic control is an ineffective intervention, but rather that treatment of hypertension should be prioritised and stressed as the most important intervention for the average population of persons with type 2 diabetes.*' Angiotensin-converting enzyme inhibitors offer no advantage over thiazide diuretics, and second-choice agents should be beta-blockers or calcium-channel blockers.

Level of evidence

(http://www.infopoems.com/levelsofevidence.cfm)
1a

Reviewed by

AS

Reference

1. Vijan S, Hayward RA. Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care. Ann Intern Med 2003; 138: 593–602.

2. Snow V, Weiss KB, Mottur-Pilson C, et al. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. Ann Intern Med 2003;1 38:587–92.

Clinical question

Are women who have a false-positive mammogram result less likely to follow-up with additional screening mammograms in the future?

Setting

Outpatient (any)

Study design

Cohort (prospective)

Synopsis

Women who have a screening mammogram yearly for 10 years have a 50% chance of having a false-positive result. This study evaluated the effect of a false-positive result on subsequent screening, using a state-wide mammography registry in Vermont. The registry includes all women in the state who receive mammograms, independent of their insurance plan or health care system. The mammogram used as the starting point (the index mammogram) was not necessarily the first mammogram the women had, but was the one that occurred during the initial enrolment period (May 1996 through May 1997).

Of the 41 844 women older than 40 years who had a mammogram, 3982 (9.6%) had a false-positive result (a number which is striking in itself). These women were younger than those in the true-negative group. False-positive results were more likely if it was the woman's first mammogram; if they had a previous mammogram, that one also was more likely to have been a false-positive (all P<.01). Women who had a false-positive result were more likely to return for a follow-up mammogram 18 months (odds ratio 1.4; 95% CI, 1.30 - 1.51) and 30 months (odds ratio 1.3; 95% CI, 1.18 - 1.44) after the index mammogram.

Bottom line

False-positive mammogram results actually increase a woman's likelihood for returning for subsequent mammography screening. Rather than getting angry with medical care that induces unnecessary anxiety, increases medical costs, and results in additional workup, women seem to be relieved that they 'dodged a bullet' after the false-positive result is refuted, though they also become more, rather than less, worried about breast cancer. Although in this case poor performance is actually good for business, we must get better at providing accurate mammography screening.

Level of evidence

(http://www.infopoems.com/levelsofevidence.cfm)
1b

Reviewed by

AS

Reference

Pinckney RG, Geller BM, Burman M, Littenberg B. Effect of false-positive mammograms on return for subsequent screening mammography. Am J Med 2003; 114:120–25.

Clinical question

Does the continuous use of combined oral contraceptives lead to less vaginal bleeding without an increase in adverse effects?

Setting

Outpatient (any)

Study design

Randomised controlled trial (nonblinded)

Synopsis

Women aged 18 to 44 years were recruited by flyer for a contraception study; the flyer did not emphasize the potential for bleeding reduction. There were 79 women enrolled and randomised (allocation concealed) to continuous (that is, no weeks off hormonal treatment) or standard 28-day cycles of 20ug ethinyl estradiol/100ug levonorgestrel (Alesse) for 48 weeks. Women who experienced prolonged bleeding of more than 10 days after cycle three (84 days) were instructed to return to the study clinic for evaluation including pelvic examination, transvaginal ultrasound, and endometrial biopsy. Weight and blood pressure were measured every 84 days. Median bleeding days in the first 84 days (cycles 1–3) were three in the continuous group and 10 in the cyclic group (P<.001). By cycles 10 to 12, 72% of women in the continuous group had no bleeding or spotting. There was a small difference in systolic blood pressure between groups at study exit among women who completed the study (116 +/- 12 mmHG standard treatment vs 108 +/- 13 continuous treatment; P=.02). Otherwise there were no differences between groups for changes in blood pressure or weight or haemoglobin. There were no pregnancies and no cases of endometrial hyperplasia or neoplasia.

Bottom line

Within six months, most women who take combination oral contraceptive pills on a continuous basis (without skipping hormonal treatment every fourth week) will not have any vaginal bleeding that requires the use of a pad. The results are similar to those of Depo-Provera, with the advantage that treatment can be stopped quickly if desired.

Level of evidence

(http://www.infopoems.com/levelsofevidence.cfm)
1b

Reviewed by

LF

Reference

Miller L, Hughes JP. Continuous combination oral contraceptive pills to eliminate withdrawal bleeding: a randomised trial. Obstet Gynecol 2003; 101:653–61.