POEMs

Patient-Oriented Evidence that Matters

The selected POEMs for April provide us with good evidence that tricyclics are more useful than SSRIs in the management of chronic low back pain, that there is a significant risk of serious bleeding when patients are started on warfarin for DVT, that prophylactic acyclovir in late pregnancy is useful for women who have a past history of genital herpes infection and that a scored two-item test is a simple and effective screening test for depression. The final POEM contains some advice about echinacea that might be useful to pass on to your patients. Editor.

Clinical question

Are antidepressants effective in the management of chronic low back pain?

Bottom line

Tricyclic and tetracyclic antidepressants that inhibit norepinephrine reuptake appear to produce moderate symptom reductions for patients with chronic low back pain. Selective serotonin reuptake inhibitors do not appear to benefit patients with chronic low back pain. None of the antidepressants seem to have much effect on functional status. (LOE=1a)

Reference

Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. Spine 2003; 28:2540–45.

Study design

Systematic review

Setting

Various (meta-analysis)

Synopsis

The authors systematically reviewed several databases looking for randomised placebo-controlled trials of oral antidepressants in managing chronic low back pain. They included studies designed to assess the treatment of multiple medical conditions if there were sufficient data to assess treatment effect on the subset with back pain. They included non-English publications. Two reviewers extracted the data, but they don't report on how discrepancies were resolved or on the degree of agreement between the reviewers. Additionally, they developed a 22-point methodologic quality-rating scale based on criteria from the Cochrane Collaboration Back Review Group and the old Agency for Health Care Policy and Research guidelines. Disagreements on the assignment of quality were resolved through consensus. The authors identified 22 trials, but excluded 15: nine lacked a placebo, three used parenteral antidepressants, two included neck and back pain without sufficient detail to extract the back pain data, and one was so poorly reported that no baseline pain data and no denominator data were available. The seven finalists included only patients with chronic low back pain. One was a placebo-controlled study of two antidepressants. The methodologic quality scores ranged from 11 to 19. Five trials evaluated norepinephrine reuptake inhibitors (amitryptilline, nortriptylline, maprotiline, imipramine). Using different assessment techniques, four reported decreases in pain, although the decreases may not have been clinically important. Only one of these studies found any effect on function. The studies using antidepressants that do not inhibit norepinephrine reuptake (paroxetine, trazodone) had negligible effects on pain or functional status.

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

Clinical question

What is the risk of bleeding in patients receiving warfarin for thromboembolism?

Bottom line

In patients taking warfarin for the treatment of a deep vein thrombosis, approximately one in 45 (2.2%) will experience a major bleeding episode, and approximately 13% of these patients will die from the bleeding. The risk of bleeding decreases after the first three months to approximately one in 54 patients (1.9%). (LOE=1a)

Reference

Linkins LA, Choi PT, Douketis JD. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism. Ann Intern Med 2003; 139:893–900.

Study design

Meta-analysis (randomised controlled trials)

Setting

Outpatient (any)

Synopsis

The authors of this meta-analysis combined the results of 29 randomised controlled trials and four prospective cohort studies. The studies were found through a search of two databases that was limited to those published in 1989 and later, since international normalised ratio (INR) was not used before 1989. Only articles in English were selected, and patients in the studies were treated with warfarin for at least three months. Two authors independently selected eligible studies; only one person extracted the data. Some of the data are a little tricky to understand; for example, to account for different lengths of treatment, the authors converted all outcomes into event rate per year. Major bleeding – bleeding that required hospitalisation, transfusion, was intracranial or into a body cavity, or was fatal – occurred in approximately one in 14 patients per year (7.22 per 100 patient-years; 95% CI, 7.19–7.24). Intracranial bleeding occurred in approximately one in every 87 patients per year (1.15 per 100 patient-years; 95% CI, 1.14–1.16), or in approximately 9% of all major bleeding episodes. In the 2422 patients who received warfarin for more than three months, major bleeding occurred in one in every 45 patients during the first three months (2.23%), followed by one in 54 patients (1.9%) over the rest of the anticoagulation period (six to 24 months). Approximately one in eight patients will die following a major bleeding episode (fatality rate = 13.4%; 95% CI, 9.4%–17.4%).

Clinical question

Does acyclovir prophylaxis prevent Caesarean deliveries due to recurrent herpes simplex virus or neonatal herpes simplex virus infections?

Bottom line

Prophylactic acyclovir (200mg four times daily or 400mg three times daily starting at 36 weeks' gestation) reduced the number of Caesarean deliveries performed because of genital herpes. It also decreased the recurrence of clinically apparent genital herpes lesions and viral shedding at the time of delivery. Since there were no cases of neonatal herpes in the study, the authors could not demonstrate an effect on that most important outcome. Less frequent dosing deserves study. (LOE=1a)

Reference

Sheffeld JS, Hollier LM, Hill JB, Stuart GS, Wndel GD. Acyclovir prophylaxis to prevent herpes simples virus recurrence at delivery: a systmatic review. Obstet Gynecol 2003; 102:1396–403.

Study design

Meta-analysis (randomised controlled trials)

Setting

Various (meta-analysis)

Synopsis

Neonatal herpes is usually due to the transmission of herpes simplex virus (HSV) from the mother around the time of delivery with up to 70% of cases associated with asymptomatic viral shedding rather than from clinically apparent lesions. The Acyclovir in Pregnancy Registry is closed since it's been determined that it's safe to take acyclovir during pregnancy. This meta-analysis of women with history of genital herpes included five randomised controlled trials with 799 patients to study prophylactic administration of acyclovir starting at 36 weeks' gestation. Clinical recurrences of HSV occurred in 4% of acyclovir-treated women and 15% of placebo-treated women (odds ratio [OR]=0.25; 95% CI, 0.15–0.40; number needed to treat [NNT]=9). The rate of Caesarean delivery because of HSV infection was essentially the same. Detection of HSV by viral culture was 0% in the acyclovir group compared with 5% in control patients (OR=0.09; 95% CI, 0.02–0.39; NNT=20). There were no cases of neonatal herpes infection in any of the studies included. Two studies used 200mg four times daily and the other three used 400mg three times daily, but there was no difference in effectiveness based on the dosing regimen.

Clinical question

Can a two-item screening questionnaire for depression be made more accurate and helpful in diagnosing depression?

Bottom line

This study expands on the idea of a two-item screen for depression by assigning a frequency score from 0 to 3 to each item. Although giving us richer information, it is also a bit more cumbersome than a simple yes or no answer. One approach to try: Screen first by asking for a simple yes or no answer (very sensitive). If a patient answers yes to either question, assess how frequently their symptoms occur. Those with a score of 5 or 6 are likely to have major depression, and those with a score of 3 or higher are likely to have any depressive disorder. Those with a score of 1 or 2 require further evaluation. (LOE=1a)

Reference

Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. Med Care 2003; 41:1284–92.

Study design

Decision rule (validation)

Setting

Outpatient (primary care)

Synopsis

This research team developed the Patient Health Questionnaire (PHQ-9), a nine-item screening device for depression. Although accurate, it is too long for practical use in the primary care setting. Others have tested and validated two-item screens that are much more practical and just as sensitive. This is a re-analysis of the original PHQ-9 data for the 580 patients who also underwent a diagnostic interview as a reference standard, looking at only two items: *'Over the last two weeks, how often have you been bothered by any of the following problems: (1) little interest or pleasure in doing things, and (2) feeling down, depressed, or hopeless.'* Each item was rated from 0 to 3 for 'not at all', 'several days', 'more than half the days', and 'nearly every day'. The total PHQ-2 score therefore ranged from 0 to 6. The reference standard was an interview with a mental health professional blinded to the PHQ-9 score. The patients were typical of those seen in primary care practice (66% women; 21% ethnic minority; mean age=46 years) and were either consecutive patients or systematically selected. Seven per cent had major depression and 22% any depressive disorder.

The accuracy of the PHQ-2 varied depending on the cutoff for an abnormal score. A cutoff of two or more to screen positive for depression had a sensitivity of 93% and specificity of 74% for major depression (positive predictive value=21%), and a sensitivity of 82% and specificity of 80% for any depressive disorder (positive predictive value=48%). A cutoff of 1 or more was 98% sensitive, but only 59% specific for major depression (positive predictive value=15%), and 91% sensitive and 65% specific for any depressive disorder (positive predictive value=37). The likelihood ratio for major depression for scores from 0 to 6 were: 0.04, 0.3, 0.6, 2.9, 5.5, 10, and 48.

Clinical question

How effective and safe is echinacea in the treatment of upper respiratory tract infections in children?

Bottom line

Echinacea purpurea extract (above ground plant only), prepared and used at the doses in this study was ineffective in treating upper respiratory tract infections (URIs) in children. Although it was generally safe to use, more parents reported a rash on their child and two children had a serious allergic-type reaction. Interestingly, children using echinacea were less likely to have recurrent URI (number needed to treat=9). (LOE=1b)

Reference

Taylor JA, Weber W, Standish L, et al. Efficacy and safety of echinacea in treating upper respiratory tract infections in children. A randomized controlled trial. JAMA 2003; 290:2824–30.

Study design

Randomised controlled trial (double-blinded)

Setting

Outpatient (primary care)

Synopsis

Although the average child has six to eight colds per year, each lasting seven to 10 days, commonly used medications such as decongestants, antihistamines, and cough suppressants lack efficacy in those younger than 12 years (I should know: With five-year-old triplets, someone in my house is ALWAYS sick!). Echinacea is widely used for the prevention and treatment of URIs in adults, but there is limited data on efficacy and safety of use in children. Data were obtained and analysed on a total of 707 URIs that occurred in 407 children. At the onset of each URI, subjects were randomly given (concealed allocation assignment) either dried pressed Echinacea purpurea juice (obtained from the above-ground herb, harvested at flowering, extracted in an alcohol-free preparation combined with syrup), or identical placebo. Dosing was age-based on the recommendations of the manufacturer and was continued until all symptoms had resolved, up to a maximum of 10 days. Parents recorded the severity of symptoms and adverse events in a daily logbook. The patients, parents, practitioners and research staff were all unaware of treatment group assignment. Ninety-four per cent of the subjects were followed up for a total of four months. Using intention-to-treat analysis, there were no differences in duration of URIs or in the overall estimate of severity of URI symptoms between the two treatment groups. The sample size was large enough to have an 80% power to detect a 1.5 to two-day difference. Other over-the-counter cold remedies were administered by parents at the same rate in both groups, but antipruitics and analgesics other than acetaminophen were administered more often to children treated with echinacea (9.8% vs 5.1%; P=.03). Overall reported and measured compliance was at least 80%. After limiting the analysis to the URIs in which patients received at least 80% of the study medication (per protocol analysis), there were still no differences found between the two groups. Children assigned to echinacea were less likely to have a second URI than those in the placebo group (52.3% vs 64.4%; P=.015; number needed to treat=9). Adverse events were reported similarly in each group, although rash was reported more often in children receiving echinacea (7.1% vs 2.7%). Two children receiving echinacea had the sudden onset of stridor requiring emergency treatment with steroids.

'Most patients with chronic illness, like the rest of us, live quietly and unremarkably in the daily struggle of our living. Our pains, like our joys, are small, interior, simple. There is no great moment to the illness or the life. Yet illness, together with other forms of misery, sometimes brings a kind of passion and knowledge of the human condition, giving an edge to life. And for some patients with chronic illness pain and suffering have more to do with life – and specifically with that aspect of life which is dark and terrible and, therefore, denied – than with a disease process. Perhaps the healer and the family, like the historian of human misery, must allow themselves to hear – within the symptoms and behind the illness, especially for the complaints of those of us who are most ordinary – the wail.'

– Kleinman A. The Illness Narratives. Basic Books; 1988. p87.