POEMs

Patient-Oriented Evidence that Matters

For August we have selected some POEMs that deal with practical solutions. Hot water is best for bluebottle jellyfish stings (if only my grandmother had known), lowering homocysteine levels is not helpful, amalgam fillings are safe for children and finally, although perhaps not quite so practical, a study that questions the applicability of clinical trial results to the real world of patients. Editor.

Clinical question

Is hot water (45°C) immersion more effective than ice pack application for relief of pain caused by bluebottle jellyfish stings?

Bottom line

Immediate hot water immersion (45°C) for up to 20 minutes is significantly more effective than ice pack application for pain caused by bluebottle jellyfish (Portuguese man-of-war) stings. (LOE = 1b-)

Reference

Loten C, Stokes B, Worsley D, Seymour JE, Jiang S, Isbistergk GK. A randomized controlled trial of hot water (45 C) immersion versus ice packs for pain relief in bluebottle stings. Med J Aust 2006; 184:329-333.

Study Design

Randomised controlled trial (nonblinded)

Funding

Foundation

Allocation

Uncertain

Setting

Population-based

Synopsis

Bluebottle jellyfish (Portuguese man-of-war) stings can cause significant pain that usually resolves within one hour. Most first-aid organisations recommend the application of ice packs. To evaluate the potential effectiveness of hot water immersion (since many marine venoms are heat labile in vitro), the investigators randomised (uncertain allocation concealment) 96 patients with an apparent bluebottle sting at two beaches in eastern Australia to either hot water immersion or ice pack application. Accurate water temperature at 45°C was insured by using thermostatic mixing valves to prevent superficial burns. Patients self-reported pain levels at baseline and at 10 minutes and 20 minutes after the commencement of treatment using a visual analog scale (VAS) of 0 to 100. The primary outcome was a clinically important reduction in pain, defined as a change in millimetres on the VAS scale dependent on the baseline starting point (16mm for an initial VAS between 0–33mm; 33mm for an initial 34–66mm; and 48mm for an initial 67–100mm). One investigator microscopically evaluated adhesive tape placed over all sting sites to confirm the presence of nematocysts. Follow-up occurred for 92% of the patients at 20 minutes. Analysis was by intention to treat. At 10 minutes, 53% of the hot water group reported a clinically significant reduction in pain compared with 32% treated with an ice pack (number needed to treat [NNT] = 5; 95% CI, 3-72). At 20 minutes, 87% of the hot water group reported a clinically significant reduction in pain compared with 33% treated with an ice pack (NNT = 2; 1–3). Radiating pain also occurred significantly less with hot water and no patient suffered a burn from hot water immersion. Nematocysts were confirmed in 42 (44%) of the subjects. Hot water immersion remained significantly more effective than ice packs in an analysis of only those patients with nematocyst-confirmed stings. Itch, redness, and rash at 24 hours occurred similarly in both groups.

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

Clinical question

Is supplementation to lower homocysteine levels an effective treatment for cardiovascular disease or disease prevention?

Bottom line

Supplementation with folic acid and B vitamins is ineffective for adults 55 years and older with known cardiovascular disease (CVD) or diabetes. A second report in the same issue found that similar supplementation in patients with a recent acute myocardial infarction was not helpful and may actually increase the risk of a bad cardiovascular outcome (relative risk = 1.22; 95% CI, 1.0 - 1.5). (LOE = 1b)

Reference

Lonn E, Yusuf S, Arnold MJ, et al, for the Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators. Homocysteine lowering with folic acid and B vitamins in vascular disease. N Engl J Med 2006;354:1567-1577.

Study Design

Randomised controlled trial (double-blinded)

Funding

Government

Allocation

Concealed

Setting

Outpatient (any)

Synopsis

An elevated level of homocysteine is an independent predictor of the risk of developing CVD. The leap that many physicians and patients have made (unsubstantiated by any evidence) is that lowering homocysteine levels through the use of B vitamins and folic acid supplements will therefore prevent or treat CVD. The current study is the first to evaluate this hypothesis in a prospective, randomised trial. The authors enrolled 5522 patients older than 54 years with known coronary, cerebrovascular, or peripheral vascular disease, or diabetes plus one additional risk factor for CVD. They then randomised the patients (allocation concealed) to receive either 2.5mg folic acid, 50mg vitamin B6, and 1mg vitamin B12 or matching placebo daily. Patients came from countries in which folate fortification of food is mandatory (United States and Canada) and not mandatory (Brazil, Western Europe, and Slovakia). Compliance with treatment was good: More than 90% and patients were followed up for a mean of five years. Groups were balanced at the start of the study and analysis was by intention to treat. As expected, homocysteine levels dropped and vitamin levels increased in the active treatment group. However, there was no difference between groups in the combined risk of cardiovascular death, myocardial infarction, or stroke (18.8% vs 19.8%; relative risk = 0.95; 95% CI, 0.84 - 1.07). There was also no difference regarding this combination of outcomes in patients in the top tertile of homocysteine levels (23.9% vs 24%). There was no difference in outcomes between countries that did or did not fortify foods with folate. Regarding individual outcomes, there were slightly fewer strokes (4.0% vs 5.3%), but more hospitalisations for unstable angina (9.7% vs 7.9%) with supplementation. The study was powered to detect a 17% to 20% relative reduction in the risk of the primary outcome. A second report in the same issue of the journal also failed to find any benefit for secondary prevention of cardiovascular events in patients with a recent acute myocardial infarction (N Engl J Med 2006;345:1578-1588). In fact, they found evidence of possible harm from B vitamin supplementation in this group of high-risk patients.

Clinical question

Are amalgam dental restorations containing mercury safe for children?

Bottom line

Children who received dental restorative treatment with amalgam did not score significantly better or worse on neurobehavioral and neuropsychological assessments than children who received resin composite material. Children who receive restoration with resin may be more likely to need additional treatment. Studies evaluating outcomes for longer than five to seven years are needed. (LOE = 1b-)

Reference

Bellinger DC, Trachtenberg F, Barregard L, et al. Neuropsychological and renal effects of dental amalgam in children. A randomized clinical trial. JAMA 2006; 295:1775-1783.

Study Design

Randomised controlled trial (double-blinded)

Funding

Government

Allocation

Concealed

Setting

Population-based

Synopsis

Health risks associated with inhalation of mercury vapor released during amalgam dental restoration are unknown. The investigators identified 534 children, aged six to 10 years, with no known prior or existing amalgam restorations and at least two posterior teeth with dental caries requiring restoration. Eligible subjects randomly (concealed allocation assignment) underwent restoration with standard amalgam containing 50% elemental mercury or with a resin composite material (white filling) free of mercury. All individuals assessing outcomes remained blinded to treatment group assignment. Complete outcome data were available for at least 75% of enrolled children during the five-year trial period, with an equal number of children unavailable in both treatment groups. Full assessment of intelligence, auditory memory, visual-motor integration, attention, and emotional state using previously validated scoring tools occurred at baseline prior to caries restoration, and at three years and five years. Children had a mean of 15 tooth surfaces restored during the five-year period. Using intention-to-treat analysis, no statistically significant differences were found between children in the amalgam group and the composite group in any of the outcomes measured. Interestingly, there was a nonsignificant increase in IQ detected in children assigned to the amalgam group. The study was 80% powered to detect a 3-point difference in IQ scores between the treatment groups. A similar seven-year randomised trial enrolling 507 children from another setting published in the same journal issue (DeRouen TA, Martin MD, Leroux BG, et al. JAMA 2006;295:1784-1792) also reported no significant differences in neurobehavioral assessments between children receiving dental restorative treatment with amalgam and those receiving a resin composite. In the second study, children assigned to restoration with resin composite were more likely to require additional restorative treatment.

Clinical question

Are cancer trial participants representative of cancer patients in the real world?

Bottom line

Patients participating in cancer trials are generally younger and healthier than those who don't participate. Their survival rates aren't necessarily better, however. This study is one of several that question the applicability of clinical trial results to real world patients. (LOE = 2b)

Reference

Elting LS, Cooksley C, Bekele BN, et al. Generalizability of cancer clinical trial results: prognostic differences between participants and nonparticipants. Cancer 2006;106:2452-2458.

Study Design

Cohort (retrospective)

Funding

Foundation

Setting

Outpatient (specialty)

Synopsis

Since fewer than 5% of cancer patients participate in clinical trials, the generalisability of the data to all cancer patients is potentially problematic. To evaluate this, the authors used data from a cancer registry that included more than 60 000 patients given a diagnosis between 1990 and 1997. To be included, they had to have undergone at least seven years of follow-up. The authors determined if the patients participated in a therapeutic clinical trial within four months of diagnosis (early participant), more than four months after diagnosis (late participants), or not at all (nonparticipants). The primary outcome was survival status by the end of 2001. The researchers also assessed the presence of comorbidity, a number of markers of disease severity, and demographic variables to determine their interrelationship with survival. After excluding patients with multiple cancers and those who had already started treatment, more than 19 000 patients were eligible for this study (5122 early participants, 1199 late participants, 13 019 nonparticipants). The participants were younger, less likely to have chronic comorbid conditions, and were more functional than nonparticipants. However, participants tended to have more distant metastasis and lymph node involvement. After taking the above-mentioned confounding factors into account, participants with localised disease had significantly shorter survival than nonparticipants. Late participants fared even worse. Participants with metastatic disease had significantly longer survival.