Oral vitamin D3 decreases fracture risk in the elderly

Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. BMJ 2003;326:469–472.

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PRACTICE RECOMMENDATIONS

Vitamin D3 (or its physiologic equivalent, ergocalciferol), administered at a dose of 100,000 IU every 4 months for 5 years, is effective for primary prevention of fractures in the active elderly aged 65 to 85 years.

This treatment regimen has no effect on cardiovascular, cancer, or all-cause mortality. Despite a seemingly large dose averaging 800 IU per day, this regimen is a safe, cheap (<$2 per year), and effective therapy for primary prevention of fractures.

BACKGROUND

Previous studies have shown that daily supplementation with vitamin D3 (800 IU) and calcium decreases the incidence of fractures; however, conflicting data exist as to whether vitamin D3 alone has the same effect. Observational studies suggest that vitamin D may increase the incidence of cancer and cardiovascular disease.

This study compares fracture risk, self-reported health and falls, incidence of cardiovascular disease and cancer, and mortality by cause for patients taking 100,000 IU of vitamin D3 orally every 4 months, compared with patients taking placebo.

POPULATION STUDIED

This British study invited 9582 doctors from the Clinical Trials Studies Unit in Oxford and 1538 patients from a general practice in Ipswich, Suffolk, aged 65 to 85 years, to participate.

Patients were excluded if they were already taking vitamin D or had contraindications to vitamin D. Of all invited people, 2037 men and 649 women were eligible and agreed to participate.

No statistical tests were performed on the characteristics of these patients, though the average age (75 years), smoking, activity, calcium intake, steroid use, hormone replacement therapy, and alcohol intake of the patients were similar in the 2 groups. Race was not reported. Nearly 90% of patients reported being active or moderately active.

STUDY DESIGN AND VALIDITY

After age, sex, and patient/physician stratification, subjects were randomly assigned to receive identical-appearing pills of vitamin D3 (100,000 IU) or placebo, which were mailed to them every 4 months for 5 years. Patients mailed back a card to confirm compliance and to report health and falls.

Analysis was by intention-to-treat. Crude outcome rates were reported, and Cox regression

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What is a POEM?

Each month, the POEMs (Patient-Oriented Evidence that Matters) editorial team reviews 105 research journals in many specialties, and selects and evaluates studies that investigate important primary care problems, measure meaningful outcomes, and have the potential to change the way medicine is practiced. Each POEM offers a Practice Recommendation and summarizes the study's objective, patient population, study design and validity, and results. The collected POEMs are available online at www.jfponline.com.

was used to calculate age-adjusted risk for fracture, cardiovascular disease and cancer, self-reported health and falls, and mortality by cause.

Patients, clinicians, and researchers were blinded to the treatment. Seventy-seven percent of patients were followed for the entire 5 years of the study. Randomization was double-blinded, and the researchers enrolling patients were not aware of the group to which the patient would be assigned (allocation was concealed).

The methodology of the study was sound. Strengths: large sample size, reasonable follow-up period, use of mortality registries for completeness, high compliance, and intention-to-treat analysis. Weaknesses were few: lack of information on race, no report of adverse effects, and lack of power calculations.

OUTCOMES MEASURED

The primary outcome was any fracture as assessed by self-report or death certificate. Secondary outcomes included self-reported health and falls, cardiovascular and cancer incidence and mortality, and all-cause mortality.

RESULTS

Compliance was similar among the physician and patient groups and between the placebo and vitamin D groups; fracture rates were similar among the physician and patient groups. Average calcium intake was similar.

The 5-year overall, age-adjusted fracture risk was lower for the patients receiving vitamin D (relative risk [RR]=0.78; 95% confidence interval [CI]=0.61–0.99; number needed to treat [NNT] for 5 years=44). Important fractures were also significantly lower—that is, those occurring at the hip, wrist, forearm, or vertebrae (RR=0.67; 95% CI=0.48–0.93; NNT for 5 years=49).

In an analysis by gender, women had a larger decrease in fracture risk at any site (RR=0.68; 95% CI, 0.46–1.01; NNT for 5 years=20). The difference for men was not statistically significant, but the study may not have enrolled enough men to find a difference if one existed.

Hip fractures, a known cause of severe morbidity in the elderly, were not significantly lower in the treated group; again, the study was probably too small or too brief to find a difference if one existed.

With respect to secondary outcomes, the vitamin D group, compared with the placebo group, had no statistically significant difference in self-reported health and falls, or mortality from cardiovascular disease, cancer, or all causes.

Analgesics do not interfere with diagnosing abdominal pain

Thomas SH, Silen W. Effect on diagnostic efficiency of analgesia for undifferentiated abdominal pain. Br J Surg 2003; 90:5–9.

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PRACTICE RECOMMENDATIONS

Despite the limitations in this review, it seems appropriate to administer analgesics to patients with generalized abdominal pain, even before a surgical evaluation. Surgeons can be assured that they will not be misled as a result of analgesia.

BACKGROUND

For years physicians have withheld pain medication from patients with abdominal pain to avoid interfering with a surgical evaluation. This recommendation can be traced back to the early 20th century and has, until recently, appeared in Sir Zachary Cope's textbook on abdominal pain.

POPULATION STUDIED

Eight randomized controlled trials were included in this review, enrolling more than 600 patients. Most were adults with undifferentiated abdominal pain. One study focused on patients between ages 5 and 18 years; one looked only at patients

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with suspected appendicitis. The settings were emergency rooms or inpatient wards.

STUDY DESIGN AND VALIDITY

The authors performed a MEDLINE search in April 2002 and identified other studies based on subsequent bibliographies. They did not search other databases or attempt to include unpublished trials.

Studies were included if they were randomized controlled trials and assessed the effects of administration of analgesics on the physical examination, diagnostic endpoints, or both. Excluded studies were not described. The authors did not describe independent searching methods or independent validity assessments.

While the authors did not explain how they assessed overall study quality, they did include comments on specific limitations in the studies. Due to the differences (heterogeneity) between trials, data were not pooled. Overall, the narrow search methods and lack of validity assessment make this systematic review somewhat weak.

OUTCOMES MEASURED

All studies included pain relief as an endpoint. Most used a 10-cm visual analog pain scale.

In addition, studies evaluated the effects of analgesics on the physical examination and diagnostic endpoints. Physical examination endpoints included presence of tenderness, peritoneal signs, and rebound. Studies also evaluated diagnostic accuracy, formulation of plans (including decision for surgery), and adverse patient outcomes.

RESULTS

In all but 1 study, analgesics were found to produce a statistically significant reduction in pain. No significant side effects, including respiratory depression or cardiovascular compromise, were noted by patients or physicians.

These studies did not find a significant difference in physical examinations or diagnostic endpoints after administering analgesics. Although 1 study found a difference in the number of tender areas when evaluated by pediatric emergency room physicians, the surgeons did not perceive this difference. Other studies showed a difference in tenderness and localization after analgesic use, but no differences in peritoneal signs and rebound.

Furthermore, no differences were found in operative decision making, and no untoward outcomes were noted between groups. No statistical power calculations were given for the above results. However, 1 study did estimate that at least 1500 patients would need to be studied to reach statistical significance in measuring untoward effects.

ACE inhibitors are better than diuretics for treatment of hypertension in the elderly

Wing LM, Reid CM, Ryan P, et al. A comparison of outcomes with angiotensin-converting-enzyme inhibitors and diuretics for hypertension in the elderly. N Engl J Med 2003; 348:583–592.

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PRACTICE RECOMMENDATIONS

Despite similar reductions in blood pressure, angiotensin-converting enzyme (ACE) inhibitors demonstrate lower combined rates of cardiovascular events or all-cause mortality in elderly hypertensive patients compared with diuretics. This benefit is most evident in men.

These results may differ from those of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) trial because that study included younger patients, had a greater representation of patients with African ancestry, used different brands of medication, and had a slightly different primary outcome. Despite these differences, both treatments offer an inexpensive means for reducing blood pressure and preventing hypertension-related complications.

BACKGROUND

The recent ALLHAT study compared the diuretic chlorthalidone with the ACE inhibitor lisinopril and the calcium-channel blocker amlodipine for treating hypertension in patients aged 55 years and older who had at least 1 other coronary heart disease risk factor.[1]

Although there was no difference in rates of fatal coronary heart disease or nonfatal myocardial infarction, chlorthalidone significantly reduced the risk of combined cardiovascular disease, stroke, and heart failure compared with lisinopril. This study compared enalapril with hydrochlorothiazide in elderly patients with hypertension.

POPULATION STUDIED

A total of 6083 subjects with hypertension, aged 65 to 84 years and mostly of European ancestry, were enrolled from 1594 family medical practices throughout Australia. Hypertension was defined as an average of 2 systolic blood pressure readings of at least 160 mm Hg, or an average diastolic blood pressure of at least 90 mm Hg with a systolic blood pressure of at least 140 mm Hg.

Exclusion criteria included a cardiovascular event within the previous 6 months, any life-threatening illness, a contraindication to an ACE inhibitor or diuretic, plasma creatinine >2.5 mg/dL, malignant hypertension, and dementia. Sixty-two percent of the patients were already being treated for hypertension.

STUDY DESIGN AND VALIDITY

In this randomized, nonblinded study, subjects were followed for a median of 4.1 years, with a blinded assessment of endpoints. Allocation was concealed. Previous antihypertensive drug therapy was discontinued at least 1 week prior to entry.

Subjects were randomly assigned to receive either ACE inhibitor or diuretic. Enalapril and hydrochlorothiazide were recommended for each of these groups, respectively; however, the specific drug decision within each class and the dosage was made by the family practitioner.

Doctors tried to achieve a 20 mm Hg reduction in systolic blood pressure to <160 mm Hg, and a 10 mm Hg reduction in the diastolic blood pressure to <90 mm Hg. A lower blood pressure was encouraged if tolerated by the subject. To reach these targets, the addition of beta-blockers, calcium-channel blockers, and alpha-blockers was recommended in both groups. Endpoints were evaluated and documented every 6 months by reviewing case records, hospital notes, and death certificates.

Overall, this was a well-designed study. The unblinded conduct of this study could be a source of bias, but would not likely be of great significance since the outcomes were primarily objective and measured by blinded assessors. The lack of representation of patients with African ancestry limits the application of the results, and may be one of the reasons for the discrepancy between these results and the results found in the ALLHAT study. The broad inclusion criteria and limited exclusion criteria strengthens the generalizability of these results.

OUTCOMES MEASURED

The primary endpoint was the combined rate of all cardiovascular events or death from any cause. Investigators also measured blood pressure and cause-specific cardiovascular events (fatal and nonfatal).

RESULTS

By the study's end, approximately 60% of the subjects were still receiving their assigned treatment. Sixty-five percent of the ACE inhibitor group and 67% of the diuretic group were receiving monotherapy. The reduction of blood pressure was similar in both groups.

The overall rate of cardiovascular events or death from any cause was lower, but not statistically significant, in the ACE inhibitor group when compared with the diuretic group (hazard ratio=0.89; 95% confidence interval [CI], 0.79–1.00; P=.05; number needed to treat=27). However, these outcomes were significantly

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lower in the male subgroup (hazard ratio= 0.83; 95% CI, 0.71–0.97; *P*=.02).

The ACE inhibitor group also showed a trend towards reduced rates of first cardiovascular events (hazard ratio=0.88; 95% CI, 0.77–1.01; *P*=.07). The ACE inhibitor group had a 32% reduction in the rate of nonfatal myocardial infarction. Fatal stroke rates remained higher in the ACE inhibitor group (hazard ratio=1.91; 95% CI, 1.04–3.50; *P*=.04; number needed to harm=91).

REFERENCE

1. Furberg CD, Wright JT, Davis BR, et al. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic (ALLHAT). *JAMA* 2002; 288:2981–2997.

Not all fish products prevent heart disease

Mozaffarian D, Lemaitre RN, Kuller LH, Burke GL, Tracy RP, Siscovick DS. Cardiac benefits of fish consumption may depend on the type of fish meal consumed. Circulation 2003; 107:1372–1377.

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PRACTICE RECOMMENDATIONS

For patients aged >65 years, modest consumption of tuna and other broiled/baked fish is associated with a lower risk of death from ischemic heart disease and fatal arrhythmias. The same is not true of fried fish or fish burgers. Instruct patients that not all fish products provide the same health effects.

BACKGROUND

The protective effect of fish consumption on fatal ischemic heart disease may be related to the effects of omega-3 polyunsaturated fatty acids, which are thought to have an anti-arrhythmic effect. The content of omega-3 fatty acids in fish varies widely, and is an order of magnitude higher in fatty fish (salmon, tuna) than in leaner fish (catfish, cod). Frying may also alter the omega-3 fatty acid content. This study investigated the relationship between consumption of different types of fish and ischemic heart disease risk.

POPULATION STUDIED

Researchers randomly selected and enrolled 5201 people aged >65 years from 4 US communities in 1989 and 1990. They excluded about 1200 subjects with known ischemic heart disease at baseline, and another 75 who failed to complete the dietary survey, leaving 3910 subjects.

The average age was 72 years; 61% were female and almost 95% were white (an additional 687 nonwhite patients were recruited at a later date, but were not included in the analysis as they did not have baseline food-frequency data). About 66% of the subjects ate tuna or other broiled or baked fish at least once per week.

STUDY DESIGN AND VALIDITY

This was a population-based prospective cohort study. Subjects responded to a picture-sort food frequency questionnaire at baseline to assess usual intake of fried fish/fish burger, tuna fish/salad/casserole, and other broiled or baked fish. Responses were in 5 categories, ranging from <5 times per year to ≥5 times per week.

As expected, serum biomarkers of omega-3 polyunsaturated fatty acid intake in a sample of 56 subjects correlated with tuna and baked/broiled other fish intake, but not with fried fish/fish burger intake. Consumption of tuna and other baked/broiled fish and the outcomes of participants in these 2 groups were closely correlated, so they were analyzed together. Annual exams, 6-month telephone interviews, medical records, and administrative databases helped to identify ischemic heart disease events.

Although the study does not explicitly mention how many subjects were lost to follow-up, the mean duration of follow-up was 9.3 years as compared with a maximum of 11.5 years, indicating

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follow-up on at least 80% of subjects. Those with higher consumption of tuna and other baked/broiled fish were more likely to be female, white, and better educated; had higher consumption of fruits and vegetables; and were less likely to smoke or have diabetes. However, the investigators adjusted the results for these and many other potential confounders.

OUTCOMES MEASURED

Primary outcomes included total ischemic heart disease death and nonfatal myocardial infarction. Also examined was the subset of ischemic heart disease deaths attributed to arrhythmias.

RESULTS

The subjects ate an average of 2.2 servings of tuna and other baked/broiled fish and 0.7 servings of fish burgers per week. Consumption of tuna and other baked/broiled fish was associated with a lower risk of death from ischemic heart disease and fatal arrhythmia, but had no effect on the risk of nonfatal myocardial infarction. The risk of death decreased progressively as consumption increased from less than 1 monthly serving to at least 3 weekly servings (hazard ratio=0.47; 95% confidence interval, 0.27–0.82).

The effects of tuna and other baked/broiled fish consumption reached statistical significance at 1 serving per week. Fish burger consumption was associated with trends toward greater risk for all 3 outcomes, but these did not reach statistical significance.

Using the unadjusted figures provided by the authors, there were 39 ischemic heart disease deaths and 22 deaths from arrhythmias in 3324 person-years of less than monthly tuna, and 39 ischemic heart disease and 17 arrhythmic deaths in 11593 person-years of thrice-weekly tuna. This translates to about 120 person-years of eating 3 or more servings per week of tuna or other baked/broiled fish instead of eating less than 1 serving per month to prevent 1 ischemic heart disease death.

Cognitive behavioral therapy and exercise minimally help Gulf War veterans' illnesses

Donta ST, Clauw DJ, Engel CC et al. Cognitive behavioral therapy and aerobic exercise for Gulf War veterans' illnesses: A randomized controlled trial. JAMA 2003; 289;1396–1404.

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PRACTICE RECOMMENDATIONS

Cognitive behavioral therapy and aerobic exercise provide only modest relief from symptoms of Gulf War veterans' illnesses. Unfortunately, over 80% of the patients showed no improvement of symptoms after 1 year of either or both treatments. With the Iraqi war ending, the outcomes of veterans of this previous conflict may prove significant.

BACKGROUND

Many Gulf War veterans have reported persistent pain, fatigue, and cognitive problems. This multisystem complex is similar to, and cannot be clinically distinguished from, other chronic multisystem illnesses such as chronic fatigue syndrome and fibromyalgia. These other illnesses have been successfully treated by cognitive behavioral therapy and aerobic exercise.

POPULATION STUDIED

This Veteran's Administration cooperative study enrolled veterans who were deployed to the Gulf War between August 1990 and August 1991 and complained of at least 2 of the following 3 symptoms: fatigue, musculoskeletal pain involving 2 or more regions of the body, and cognitive symptoms (memory, concentration, or attention difficulties). These symptoms must have begun after August 1990, lasted for more than 6 months, and persisted at the time of screening.

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Only exercise showed significant improvement among subjects with Gulf War veterans' illnesses

Veterans were excluded from enrollment by any 1 of the following: physical impairment precluding exercise or cognitive behavioral therapy; past cognitive behavioral therapy for Gulf War veterans' illnesses; concurrent enrollment in another clinical trial; pregnancy; clearly defined disease that accounts for the veteran's symptoms; severe psychiatric illness; activity level rated at greater than 7 metabolic equivalents; score of ≥40 on the physical component summary of the Short Form Health Survey for Veterans. (A low physical component summary score implies poor physical conditioning.)

Eighty percent of enrollees had all 3 cardinal symptoms of Gulf War veterans' illnesses. Mean age was 40.7 years old (standard deviation, 8.7 years), 15% were female, and mean duration of symptoms was 6.7 years. These veterans have symptoms similar to those exhibited by patients of family physicians.

STUDY DESIGN AND VALIDITY

Subjects were randomized to 1 of 4 treatment groups: usual care, cognitive behavioral therapy plus usual care, aerobic exercise plus usual care, and cognitive behavioral therapy and aerobic exercise plus usual care. Cognitive behavioral therapy or exercise groups met 1 hour per week for 12 weeks.

Follow-up assessments by research personnel blind to treatment group assignment were performed immediately after the groups ended at 3 months, and then at 6 and 12 months. Nurses called subjects monthly to check on adherence to their individualized home programs, which were given at the final group meeting. The researchers used a modified intention-to-treat analysis with a generalized linear mixed model.

The strengths of this study were randomization using concealed allocation assignment, group make-up, and large group size. The weaknesses were the unclear definition of Gulf War veterans' illnesses, no clear model of behavioral or cognitive factors of the illnesses, subjects enrolled with pre-existing chronic fatigue syndrome and fibromyalgia, duration of symptoms prior to the study, and high percentages of veterans enrolled with disabilities and psychological or psychiatric illnesses.

OUTCOMES MEASURED

The primary outcome was the percentage of veterans who improved more than 7 points on the physical component summary compared with baseline. Secondary outcomes were changes in the self-measurements of pain, fatigue, cognitive difficulties, physical conditioning, and mental health-related functioning.

RESULTS

Ninety-one percent of subjects completed the 12-month follow-up visit. No significant differences in the primary outcome (physical component summary score) were found between treatment groups when correcting for multiple measurements. Only exercise alone showed a significantly higher (P=.02) improvement among adherent subjects (attending 8 or more weekly meetings) compared with nonadherent subjects.

Veterans who underwent cognitive behavioral therapy had improved symptoms compared with those who did not (odds ratio=1.71; 95% confidence interval, 1.21–2.41; number needed to treat=15).

Secondary outcomes showed no significant difference in mean adjusted scores relative to baseline for any of the treatment arms. At the statistically different level of 0.025, mental component summary and cognitive symptoms improved with cognitive behavioral therapy.

All 5 measures of fatigue and distress exhibited statistically significant improvement with aerobic exercise. Neither treatment had any significant effect on pain.

Admission electronic fetal monitoring does not improve neonatal outcomes

Impey L, Reynolds M, MacQuillan K, Gates S, Murphy J, Sheil O. Admission cardiotocography: a randomized trial. Lancet 2003;361:465–470.

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PRACTICE RECOMMENDATIONS

Admission electronic fetal monitoring did not decrease neonatal morbidity and mortality compared with intermittent auscultation.

Patients in the admission fetal monitoring group were more likely to receive continuous electronic monitoring and fetal blood sampling, but there were no significant differences in the rates of operative deliveries or episiotomy. Institutions not routinely using admission electronic fetal monitoring should not start; those that do may not be benefiting their patients.

BACKGROUND

No studies have been able to demonstrate that routine electronic fetal monitoring decreases fetal birth asphyxia or its attending complications, such as cerebral palsy. Electronic fetal monitoring is still, however, the main mode of monitoring labors thought to be at high risk of intrapartum asphyxia. Admission electronic fetal monitoring has been used as an attempt to identify high-risk labors that might benefit from continuous electronic fetal monitoring during labor.

POPULATION STUDIED

Women were eligible for inclusion if they were admitted in labor and would not have otherwise undergone routine continuous electronic fetal monitoring. Inclusion criteria were singleton gestation <42 weeks, no concern for antenatal fetal compromise, no adverse obstetrical history, clear amniotic fluid, and no maternal fever.

STUDY DESIGN AND VALIDITY

Immediately after early amniotomy on diagnosis of labor, 8628 eligible women were randomized to receive either 20 minutes of external fetal monitoring or usual care (intermittent auscultation only). If the admission monitoring showed a baseline heart rate of 110 to 160 beats/min, acceptable variability, no decelerations, and more than 1 acceleration, intervention group patients received intermittent auscultation. If these criteria were not met, then electronic fetal monitoring was continued until delivery.

Usual-care patients received continuous electronic fetal monitoring only if there was deceleration in fetal heart rate, persistent fetal tachycardia, meconium or heavy blood staining in amniotic fluid, maternal fever, or labor lasting longer than 8 hours.

Concealed allocation assignment was accomplished with the use of sealed, opaque envelopes. Analysis was by intention-to-treat, and individuals assessing outcomes were blind to treatment group assignment. All women in the study had early amniotomy, and all nulliparous women had their labor actively managed.

OUTCOMES MEASURED

The primary outcomes measured were neonatal mortality in the absence of a major congenital malformation or moderate-to-severe morbidity (admission of an infant to the neonatal intensive care unit with cord-blood metabolic acidosis, neonatal seizures, hypotonia lasting >4 hours, mechanical ventilation >15 minutes, use of inotropic support, renal failure, or meconium aspiration syndrome).

Secondary neonatal outcomes were admission to the neonatal intensive care unit and length of stay, mean arterial/venous pH and base deficit, Apgar scores, and postnatal imaging. Maternal secondary outcomes were the use of continuous electronic fetal monitoring, fetal blood sampling,

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rates of cesarean delivery, instrumental delivery and episiotomy, and mean estimated blood loss.

RESULTS

There was no difference in the primary outcome of neonatal morbidity and mortality between the intervention and usual-care groups (1.30% vs 1.28%). There were no differences in the groups for any of the neonatal secondary outcomes.

More women in the admission electronic fetal monitoring group received continuous electronic fetal monitoring (58% vs 42%; relative risk [RR]=1.39; 95% confidence interval [CI], 1.33–1.45) and fetal blood sampling (11% vs 8%; RR=1.30; 95% CI, 1.14–1.47) than in the usual-care group.

Rates of cesarean section, instrumental delivery, and episiotomy did not differ between groups. This study had adequate power to show a decrease in serious neonatal mortality of 50%, but some clinicians might consider a 25% reduction enough to justify using admission electronic fetal monitoring.

Is terazosin helpful in chronic prostatitis?

Cheah PY, Liong ML, Yuen KH, et al. Terazosin therapy for chronic prostatitis/chronic pelvic pain syndrome: A randomized, placebo controlled trial. J Urology 2003; 169:592–596.

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PRACTICE RECOMMENDATIONS

Terazosin, an alpha-1-adrenergic blocker, is well tolerated, relieves pain symptoms, and improves quality of life in healthy men aged 20 to 50 years who have chronic prostatitis/chronic pelvic pain syndrome.

Terazosin should be strongly considered as a first-line treatment in such patients. However, men with infectious prostatitis were excluded from this study. Also, the benefits of terazosin beyond 14 weeks are unknown.

BACKGROUND

Lifetime prevalence of chronic prostatitis in men aged 40 to 79 years is 5%, resulting in significant morbidity, unnecessary antibiotic use, and both patient and physician frustration.[1] The vast majority of cases of chronic prostatitis are nonbacterial, recently termed chronic prostatitis/chronic pelvic pain syndrome by the National Institutes of Health (NIH) consensus classification of prostatitis syndromes.

Studies of prostatic massage, 5α-reductase inhibitors, anti-inflammatory drugs, biofeedback, allopurinol, and surgery report either insufficient data or conflicting results, preventing recommendations for routine use. Alpha-blockers have been shown to improve disease-oriented outcomes in patients with chronic prostatitis/chronic pelvic pain syndrome.[2]

POPULATION STUDIED

One hundred men aged 20 to 50 years were recruited from hospitals in Northern Malaysia (mostly of Chinese and Malay ethnicity) during a national prostatitis awareness campaign. Eligible men met NIH criteria for chronic prostatitis, with recent pain and decreased quality of life.

Patients with chronic bacterial prostatitis, urinary tract infection within a year, significant medical problems, prior treatment with alpha-blockers, concomitant use of other prostatic medications, or use of medications potentially inhibiting lower urinary tract function were excluded.

STUDY DESIGN AND VALIDITY

Subjects were randomly assigned in double-blind fashion to receive terazosin or identical placebo. It was not possible from the text to determine if allocation assignment was concealed. Terazosin was initiated at 1 mg/d and titrated as tolerated to 5 mg/d over 2 weeks, and continued for a total of 14 weeks. Outcomes were assessed at 2, 4, and 14 weeks using intention-to-treat analysis.

The authors used the NIH Chronic Prostatitis Symptom Index (NIH-CPSI). This validated, prostate-specific index consists of 9 questions

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Terazosin should be considered a first-line therapy for patients with nonbacterial prostatitis

evaluating 3 domains of chronic prostatitis: pain and discomfort, urinary symptoms, and impact on quality of life. The ninth item on this index was chosen as the primary outcome: "If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?"

Baseline characteristics of the groups were similar for age, race, prostate size, median quality of life scores, and median NIH-CPSI pain domain scores. Mean initial prostate-specific antigen level was 0.67 ng/mL in the terazosin group vs 0.96 ng/mL in the placebo group. Patients in the placebo group reported a nonsignificantly longer duration of symptoms. Forty-three patients (86%) in each group completed all follow-up assessments.

OUTCOMES MEASURED

The primary outcome measured was the quality-of-life item on the NIH-CPSI. Patients answered the questions 0 to 6 (0=delighted, 1=pleased, 2=mostly satisfied, 3=mixed, 4=mostly dissatisfied, 5=unhappy, 6=terrible). Patients with scores of 0, 1, or 2 at week 14 were considered responders. The secondary outcome measured was a 50% or greater reduction in the NIH-CPSI pain domain score.

RESULTS

At week 14, 56% of patients receiving terazosin versus 33% receiving placebo responded to treatment (P=.03; number needed to treat [NNT]=4). More patients in the terazosin group reported a 50% decrease in pain domain scores (60% versus 37%; P=.03; NNT=4).

Other outcomes favoring terazosin therapy included both the mean NIH-CPSI total score (P=.01) and individual NIH-CPSI domain scores (P<.05). Interestingly, the groups did not differ in regards to peak urinary flow rate or postvoid residual. More adverse reactions were reported in the terazosin group; however, no patient withdrew from the study because of side effects.

REFERENCES

1. Roberts RO, Lieber MM, Rhodes T, et al. Prevalence of a physician-assigned diagnosis of prostatitis: the Olmsted County study of urinary symptoms and health status among men. *Urology* 1998; 51:578–574.
2. Collins M, MacDonald R, Wilt T. Diagnosis and treatment of chronic abacterial prostatitis: a systematic review. *Ann Intern Med* 2000; 133:367–368.

Topical ophthalmic NSAIDs reduce pain faster than placebo

Weaver CS, Terrell KM. Update: Do ophthalmic nonsteroidal anti-inflammatory drugs reduce the pain associated with simple corneal abrasion without delaying healing? Ann Emerg Med 2003; 41:134–140.

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PRACTICE RECOMMENDATIONS

Topical ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) relieve the pain of uncomplicated acute corneal abrasions faster than placebo eyedrops.

The pain relief is small; whether the pain relief difference would be noticed by patients and how it compares with oral analgesics is unknown. Given the cost of topical NSAIDs, they are most useful for a select patient population: those who must return to work immediately, and those for whom opioid analgesia-induced sedation is intolerable.

BACKGROUND

Corneal abrasions are common in primary care and emergency practices, and the pain can be quite disabling. Standard acute treatment includes cycloplegics and topical anesthetics;

patients are often discharged with oral narcotic analgesics. Topical ophthalmic NSAIDs are an alternative to oral analgesics.

POPULATION STUDIED

The authors reviewed the use of topical ophthalmic NSAIDs for simple corneal abrasions in adult patients presenting to emergency departments. Two studies were performed in the United States; 3 in Europe. Exclusion criteria were serious injuries or complicating factors including other eye pathology, use of contact lenses, and pregnancy. Gender, race, and median age of subjects were not provided.

STUDY DESIGN AND VALIDITY

This critical appraisal update searched only English-language databases available through OVID and found 6 randomized double-blinded studies comparing NSAIDs with placebo topical ophthalmic solutions, containing either ketorolac, diclofenac, or indomethacin. One study was not included because it used contact lenses as a co-intervention.

The methodological quality of the studies was rated good to strong, although the rating criteria and the process of evaluation were not described. Due to the heterogeneity in pain assessment (timing and intensity measurement tool), the authors were able to provide only a qualitative summary of the 5 studies.

The sample sizes for the studies ranged from 40 to 123. It is not clear whether the smaller samples had adequate power to detect a difference in treatment effect. Four of the studies had similar treatment and control groups; information was not available for the fifth. All studies randomized patients to treatment or control groups; patients and physicians were blinded to the assignment. Allocation may not have been concealed in these studies.

At least 88% of participants completed the studies; participation ended when full corneal healing was observed. There was no dropout difference between treatment and placebo groups.

OUTCOMES MEASURED

The primary outcome was pain, measured using an analog pain scale that compared pain at baseline and at designated intervals. Two used a visual analog scale of 0 to 100, one used a visual analog scale of 0 to 5, one used a "scale" of 0 to 10, and one used a Numeric Pain Intensity Score of 0 to 10. One study noted pain intensity as soon as 1 hour after start of treatment, one study at 2 hours, and 3 studies reviewed pain relief 1 day after treatment started.

Three studies compared the rate of use of oral analgesics ("rescue" medication) between the treatment and control groups, while 4 studies also looked at an outcome of subjective, qualitative symptoms like foreign-body sensation. Only 1 study reported time to return to work.

RESULTS

Treatment and control subjects had similar corneal healing time. Based on the analog pain scales, patients receiving the NSAIDs achieved relative pain relief more quickly than those receiving placebo.

The difference in pain relief between the 2 groups was, however, in the range of questionable clinical significance (the minimum clinically significant pain difference is 13 mm on a 100-mm visual analog scale, as found in a study of trauma patients[1]).

One of the 3 studies that reported on oral analgesic use found a significant reduction of pain in the treatment group, with 16% of the treatment group and 50% of the placebo group using oral analgesics. Two studies reported a decrease in subjective, qualitative symptoms among NSAID patients; 2 found no difference. In the single study evaluating this outcome, patients receiving topical NSAIDs were able to return to work, on average, 0.6 days more quickly than patients receiving placebo.

REFERENCE

1. Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. *Ann Emerg Med* 1996; 27:485–489.

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Patients with mild scoliosis have good prognosis

Weinstein SL, Dolan LA, Spratt KF, Peterson KK, Spoonamore MJ, Ponsetti IV. Health and function of patients with untreated idiopathic scoliosis. JAMA 2003; 289:559–567.

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PRACTICE RECOMMENDATIONS

Patients with late-onset idiopathic scoliosis have only a modest increase in health problems compared with patients without scoliosis. Clinicians should keep this in mind when providing health education and offer reassurance and watchful waiting to patients with small curves at skeletal maturity.

More broadly, whether to screen for scoliosis depends on the performance of the screening test as well as evidence of whether treatment alters the natural history of scoliosis. The US Preventive Services Task Force has concluded that there is insufficient evidence to recommend routine screening.[1]

BACKGROUND

Late-onset idiopathic scoliosis arises in otherwise normal children, usually after 10 years of age. Children are often screened for scoliosis, but controversy remains about its long-term prognosis. This historical cohort study assessed the 50-year prognosis of patients with untreated late-onset idiopathic scoliosis.

POPULATION STUDIED

A total of 117 patients with late-onset scoliosis were enrolled at a university orthopedics clinic from 1932 to 1948. Patients with congenital, neuromuscular, and early-onset idiopathic scoliosis were excluded. The average age at follow-up was 66 years; 89% were women, and 97% were white.

The average Cobb angles at skeletal maturity were 61° and 35° for thoracic and lumbar curves, respectively. Thus, the patients were probably similar to most people referred from a family practice, but more detailed information about how these patients were enrolled, socioeconomic status, and other diseases would be valuable.

STUDY DESIGN AND VALIDITY

The original cohort included 444 patients; 144 of these were located and 27 refused participation. Subjects were offered questionnaires, a physical examination, and radiologic studies.

A comparison group of 62 volunteers with a negative Adams forward bend test, no history of spinal curvature, and matched by age and gender was enrolled from hospital clinics, senior citizen centers, and retirement homes. All dependent variables were tested statistically for differences due to curve type and between cases and controls. Survival was assessed by the Kaplan-Meier method and compared with United States life-tables.

The methodological strength of this study was fair. Strengths include exclusion of other causes of scoliosis and the length of follow-up. The major weakness was the poor follow-up (32%), which can greatly bias outcomes. Other weaknesses included low frequency of physical examination and radiologic testing, poor choice of controls, inattention to potentially confounding illnesses or treatments, nonblinding of evaluators, and lack of statistical power, correction for multiple tests, or assessment of confounding. Despite these flaws, however, this study provides some of the best data we have to answer this important question.

OUTCOMES MEASURED

The primary outcomes measured were mortality compared with US life-tables, prevalence of acute and chronic back pain, pulmonary symptoms, activities of daily living, depression, and body image. Quality of life and more specific functional status were not addressed.

RESULTS

Of the 117 patients, everyone completed a questionnaire, 54 had a physical exam, and 80 had

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radiographs. The average follow-up was 51 years.

There were no differences between cases and controls in activities of daily living, depression, or reported shortness of breath. For patients with relatively small curves (<80° thoracic or <50° lumbar), those with thoracic curves were at no greater risk for shortness of breath than those with lumbar curves.

Patients had more chronic back pain than controls (61% vs 35%; P=.003), although there was no difference in the intensity or duration of pain. Scoliosis patients had lower satisfaction with their body appearance (P<.001), and this extended to their entire bodies.

As for long-term prognosis, a Cobb angle of >50° at skeletal maturity was associated with development of shortness of breath (odds ratio=3.67; 95% confidence interval, 1.11–12.12). Assuming that half the patients not located were not dead, the survival probability for patients' with scoliosis was 0.55, similar to survival of women to age 65 years. This finding, however, was very dependent on assumptions about the outcomes of those not followed up.

REFERENCE

1. US Preventative Task Force. Screening for adolescent idiopathic scoliosis: policy statement. *JAMA* 1993; 269:2664–2666.

12-hour protocol safe for cocaine-associated chest pain

Weber JE, Shofer FS, Larkin GL, et al. Validation of a brief observation period for patients with cocaine-associated chest pain. N Engl J Med 2003; 348:510–517.

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PRACTICE RECOMMENDATIONS

A 12-hour emergency department observation period is safe for patients with cocaine-associated chest pain, provided they have symptoms consistent with low-to-intermediate likelihood of unstable angina according to the Braunwald classification, and normal serial troponin I levels and cardiogram.

Patients with traditional cardiac risk factors should undergo cardiac stress testing within 2 weeks following the chest pain event, as atherosclerosis enhances the vasoconstrictive effects of cocaine. All patients should be referred for substance abuse counseling, as recurrent cocaine use was associated with subsequent nonfatal myocardial infarction (MI).

BACKGROUND

In the first hour after cocaine use, there is a 24-fold increase in the risk of sustaining MI. In 2000, over $83 million was spent on hospitalization for cocaine-associated chest pain.

POPULATION STUDIED

The authors enrolled a total of 302 subjects with acute onset chest pain. The mean age for subjects was 37.6 years; 66% were male, and 70% were African-American.

This study included those aged 18 years and older if they reported cocaine use in the

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In 2000, over $83 million was spent on hospitalization for chest pain associated with cocaine use

week prior to presentation, or if the results of a toxicologic urine screening revealed cocaine metabolites; if chest discomfort was their chief symptom; and if their symptoms were consistent with low-to-intermediate likelihood of unstable angina according to the Braunwald classification.

The authors excluded subjects who had chest pain that was noncardiac or high-risk. High-risk patients were those with an initial electrocardiogram (ECG) that suggested the presence of ischemia or acute MI; ST-segment elevation or depression of 1 mm or more that persisted for at least 1 minute; elevated serum levels of cardiac markers; recurrent ischemic chest pain; or hemodynamic instability.

STUDY DESIGN AND VALIDITY

From January 1, 1998, to January 1, 2000, the authors enrolled consecutive subjects with cocaine-associated chest pain in a longitudinal cohort study. Investigators questioned subjects regarding the route and timing of cocaine use and classified the ECGs according to the degree of ischemia present.

The low-to-moderate risk subjects remained in the observation unit, where researchers measured troponin I at 0, 3, 6, and 9 hours after presentation, performed continuous ECG monitoring and toxicologic urine screening, and assessed for heart failure.

The subjects without evidence of myocardial necrosis or ischemia at rest after 9 hours of observation performed exercise stress testing according to the modified Bruce protocol. Because very few subjects had positive tests, researchers changed the protocol during the study to recommend follow-up after discharge with a physician for outpatient stress testing.

After discharge, the authors contacted subjects within at least 30 days and inquired about ventricular dysrhythmias, nonfatal MI, recurrent chest pain, and recurrent cocaine use. If the researchers were unable to directly contact a subject, they attempted to reach a contact person, and then sent a telegram. They did not ask the contact person about anything other than survival. They confirmed all adverse events with hospital records, including MI and death.

Overall, the study was well-designed. However, the authors included all subjects who reported cocaine use in the previous week. Although the exact time frame for cocaine-associated MI is not known, it is conceivable that the influence of cocaine is absent after several days, thus creating a heterogeneous population of test individuals.

Also, data regarding anything other than death is not available for nearly 15% of the subjects—so the actual number of adverse events may be greater than reported.

OUTCOMES MEASURED

The outcomes measured at 30 days included death from cardiovascular causes, ventricular dysrhythmias, nonfatal MI, recurrent chest pain, and recurrent cocaine use.

RESULTS

Outcome data were available for 300 of the 302 subjects. There were no deaths from cardiovascular causes—the 2 individuals who could not be reached for follow-up were not listed on the National Death Registry.

Of the 256 who were contacted directly, none had sustained ventricular dysrhythmias. Only 1.6% (95% confidence interval [CI], 0.1%–3.1%) of subjects had subsequent nonfatal MI—all of whom had at least 2 cardiac risk factors and subsequent cocaine use. Recurrent chest pain was reported by 24.7% (95% CI, 19.4–30.0), and 25.2% (95% CI, 19.9–30.5) reported recurrent cocaine use.