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Bisphosphonates may protect against breast cancer

Publish date: SEP 01, 2012

By: Contemporary OB/GYN Staff



Research has shown that use of bisphosphonates for bone loss may be associated with reduced risk of breast cancer recurrence, but the role of treatment duration is unclear. In fact, according to a recent meta-analysis, bisphosphonate therapy may decrease breast cancer risk for as long as treatment continues.

Investigators searched the medical literature through June 2011 for studies of the association between bisphosphonate use and breast cancer risk that included, or allowed the calculation of, relative risks (RRs) and 95% confidence intervals (CIs). Four studies were ultimately used for data

extraction and synthesis. Risk was evaluated for any use of bisphosphonates and per 1-year increase in bisphosphonate use compared with nonusers.

The publications were 2 cohort studies and 2 retrospective case-control studies from 2010 and 2011 that included a total of 15,363 breast cancer patients and 84,931 bisphosphonate users. Among the 3 studies that listed the relevant medications, alendronate was the most common bisphosphonate (52% to 90%).

Women who used any type of bisphosphonate had a 15% reduction in risk of breast cancer compared with nonusers (pooled RR 0.85; 95% CI, 0.74-0.98), and the reduction was even greater, at 32%, when the analysis was restricted to patients with invasive tumors (pooled RR 0.68; 95% CI, 0.59-0.80). A dose-response relation was found, whereby for each additional year of bisphosphonate use, women had a reduced risk of breast cancer (pooled RR 0.92; 95% CI, 0.87-0.96) compared with nonusers. The benefit seemed to appear after at least 1 year of use, which gave a significant reduction in risk ($P < 0.001$); results for treatment of less than 1 year were insignificant ($P = 0.51$).

Bisphosphonates therefore appear to reduce risk of any [breast cancer diagnosis](#) and, in particular, risk of invasive tumors. The authors acknowledge the limitations of meta-analyses and state that randomized controlled trials are needed before bisphosphonates can be prescribed for prevention of breast cancer.

Liu Y, Zhao S, Chen W, et al. Bisphosphonate use and the risk of breast cancer: a meta-analysis of published literature. *Clin Breast Cancer*. 2012;12(4):276-281.

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Obesity and diabetes may increase risk of orthopedic surgical-site infections

Publish date: SEP 01, 2012



By: Contemporary OB/GYN Staff



Diabetes is known to be associated with infectious complications after orthopedic procedures, and a recent study indicates that obesity and diabetes are independent risk factors for postoperative surgical-site infections (SSIs).

The study, performed in a Finnish hospital specializing in [joint replacement](#), explored the effects of obesity and diabetes on infection rates after primary hip and knee replacement procedures. This population-based series included 7181 hip and knee replacements performed for osteoarthritis between 2002 and 2008. Plasma glucose was measured repeatedly before and during the hospital stay, and hyperglycemia was defined as glucose ≥ 6.9 mmol/L (124 mg/dL). Patients were evaluated prospectively for the occurrence of periprosthetic joint infection during the year after surgery.

Joint infections were diagnosed after 52 procedures (0.72%). Morbid obesity (≥ 40 kg/m²) was associated with significantly more infections than was normal body weight (< 25 kg/m²), with infection rates of 4.66% versus 0.37%, respectively. Morbid obesity remained significant in multivariate analysis (OR 6.4; 95% CI, 1.7-24.6), although intermediate levels of obesity (25-29, 30-34, and 35-59 kg/m²) were not significant. Hip replacements in morbidly obese patients were associated with a 30-fold elevation in infection risk, and knee replacements with an 8-fold increase.

Patients with diabetes diagnosed before surgery had an elevated infection risk independent of obesity (OR 2.3; 95% CI, 1.1-4.7). However, morbidly obese patients with diabetes had the highest infection rate (9.8%).

Jømsen E, Nevalainen P, Eskelinen A, Huotari K, Kalliovalkama J, Moilanen T. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for [osteoarthritis](#). *J Bone Joint Surg Am.* 2012;94(14):e1011-e1019.

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Cefixime no longer recommended for treatment of gonorrhea

Publish date: SEP 01, 2012

Print

By: Contemporary OB/GYN Staff

The spread of antimicrobial resistance has claimed another victim. According to the Centers for Disease Control and Prevention (CDC), gonorrhea should no longer be treated with cefixime as a first-line therapy. The CDC updated its treatment guidelines in the August 10 issue of *Morbidity and Mortality Weekly Report*.

Neisseria gonorrhoeae is highly prevalent and an important cause of pelvic inflammatory disease, ectopic pregnancy, infertility, and the spread of HIV infection. The CDC conducts periodic gonorrhea surveillance through its Gonococcal Isolate Surveillance Project. Laboratory studies for 2006-2011 indicate that urethral *N gonorrhoeae* has developed resistance to cefixime, which is therefore no longer recommended at any dose for first-line therapy.

Instead, the CDC states that uncomplicated urogenital, anorectal, or pharyngeal gonorrhea should be treated with combination therapy with ceftriaxone 250 mg intramuscularly plus either azithromycin in a single dose of 1 g orally or doxycycline at 100 mg orally twice a day for 1 week. Treatment failure should be addressed by culture and antimicrobial susceptibility testing. Cefixime and other medications can be considered as second-line agents, followed by a test-of-cure 1 week later. Sex partners also require treatment.

Supporting data for the new recommendations include elevations in cefixime minimum inhibitory concentrations (MICs) in men. Between 2006 and 2011, the proportion of isolates with elevated MICs (≥ 0.25 \blacklozenge g/mL) increased significantly, especially in men who have sex with men and in the western United States.

The need for the guideline revision comes as no surprise, given that *N gonorrhoeae* has previously developed resistance to fluoroquinolones, prompting the CDC to recommend cephalosporins instead, and the recent discovery of declining effectiveness of cefixime. CDC hopes that the restriction of cefixime use will also delay the development of resistance to ceftriaxone.

Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral Cephalosporins No Longer a Recommended [Treatment for](#) Gonococcal Infections. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.* 2012;61:590-594.

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Mammographic screening is proven to save lives

Publish date: OCT 01, 2012



By: Contemporary OB/GYN Staff

Some studies in the literature have questioned the benefit of mammographic screening in reducing breast cancer mortality. But a recent case-control study and meta-analysis indicate a definitive benefit for the screening in lowering such mortality rates.

The case-control study looked at data from BreastScreen Australia, a population-based [program](#) that invites women aged 50 to 69 years for free biennial mammographic screening. For the new report, investigators from Western Australia compared data on women who died of breast cancer between 1995 and 2006 (i.e., cases) with up to 10 age- and resident-matched women known to be alive on the date of a case's death (i.e., controls). The study outcome was the effect of participation in the BreastScreen program on the likelihood of death due to breast cancer. Results were reported as odds ratio (ORs) and 95% confidence interval (CIs).

The study included 427 cases and 3,650 controls. Screening was found to be more common among the controls (56%) than among the cases (39%), and the reduction in mortality risk attributed to screening was statistically significant (adjusted OR 0.48; 95% CI, 0.38-0.59). The results did not differ markedly for subgroups of year at death (1995-1997, 1998-2001, or 2002-2006) or for age at the study reference date (50-59 or 60-69 years).

A review of the literature yielded 9 other case-control studies on [breast cancer screening](#) and mortality, which included women from Australia, Iceland, Italy, the Netherlands, the United Kingdom, and Wales. Meta-analysis confirmed a significant reduction in breast cancer mortality among screened women (OR 0.51; 95% CI, 0.46-0.56). The results were similar when the data were analyzed separately by country.

This study indicates that mammographic screening cuts the risk of breast cancer mortality in half. The case-control study found approximately a 52% reduction in breast cancer mortality in the BreastScreen Australia program, versus 49% in the meta-analysis. These results corroborate those from a previous case-control study on the BreastScreen Australia program. The authors conclude, "screening is of benefit to women who choose to be screened."

Nickson C, Mason KE, English DR, Kavanagh AM. Mammographic screening and breast cancer mortality: a case-control study and meta-analysis. *Cancer Epidemiol Biomarkers Prev.* 2012;21:1479-1488.

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Snapshot

In this protocol, Dr. Higgins reviews the pathophysiology, diagnosis, and treatment of hypoxic ischemic encephalopathy (HIE).

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Benefits outweigh risks of newborn male circumcision

Publish date: OCT 01, 2012



By: Contemporary OB/GYN Staff

Circumcision of male infants provides benefits that outweigh the risks, according to a recent [policy statement](#) from the Task Force on Circumcision of the American Academy of Pediatrics (AAP) endorsed by the American College of Obstetricians and Gynecologists (ACOG).

A multidisciplinary workgroup convened by the AAP to update recommendations from 1999 reviewed the benefits and risks of newborn male circumcision in 2007. Participants included the AAP, the American Academy of Family Physicians, ACOG, and the US Centers for Disease Control and Prevention. Evidence was gathered through a review of the medical literature from 1995 through 2010.

Circumcision, the Task Force members noted, helps prevent [urinary tract infection](#) early in life and HIV infection, human papillomavirus infection, genital herpes, and penile cancer later in life and reduces transmission of certain sexually transmitted diseases and risk of cervical cancer in sex partners. Evidence shows that circumcision does not impair sexual function or satisfaction but it must be performed by someone properly trained because complications—albeit rare—are more likely with inexperienced surgeons. Sterile operative technique and pain management are mandatory to ensure that infants tolerate the procedure well. The Task Force also noted that circumcision is more beneficial and safer when performed in newborns than later in life.

The health benefits of circumcision, while significant, were not considered critical enough by Task Force members to mandate routine circumcision of all newborns; therefore, the procedure is still elective. Other considerations may include religious, cultural, and ethical beliefs. Families need accurate and unbiased information on the benefits and risks of circumcision and should have access to the procedure—and insurance reimbursement for it. The decision about circumcision ideally should be made before conception or in early pregnancy. The Task Force recommended development of educational materials for both parents and healthcare professionals to ensure that practitioners are comfortable discussing the topic with parents.

The Task Force concluded, "Evaluation of current evidence indicates that the health benefits of newborn male circumcision outweigh the risks and that the procedure's benefits justify access to this procedure for families who choose it." ACOG has endorsed these conclusions of the AAP Task Force on Circumcision.

Task Force on Circumcision. Circumcision policy statement. *Pediatrics*. 2012;130(3):585-586.

Task Force on Circumcision. Male circumcision. *Pediatrics*. 2012;130(3):e756-e785.

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Genetic factors explain why women gain visceral fat more readily than men

Publish date: OCT 01, 2012



By: Contemporary OB/GYN Staff

Women and men gain weight when they eat a high-fat diet and during midlife. But many women say that gaining weight is easier and losing it is harder for them than for men. An experimental study in mice provides a genetic rationale for that difference.

Researchers at The Ohio State University studied aldehyde dehydrogenase, an enzyme that produces retinoic acid. Retinoic acid, derived from vitamin A, plays a role in formation of visceral (abdominal) fat. Mice were bred to express or to lack one type of the enzyme, Aldh1a1, and the effects on fat formation were compared in male and female mice fed a high-fat diet for nearly 1 year.

During the high-fat diet, normal mice of both sexes gained weight (specifically subcutaneous fat), but only the females were likely to also accumulate visceral fat. Other experiments indicated that female mice fed a normal diet expressed very low levels of retinoic acid but their levels of retinoic acid were strikingly higher when they were fed a high-fat diet. The result was much higher visceral fat accumulation than in males.

Male and female mice that were genetically altered to lack the enzyme Aldh1a1 and then fed a high-fat diet had a reduction in subcutaneous fat, but only the females showed resistance to visceral fat accumulation, even with high caloric intake. The explanation is likely to be that the females were no longer producing retinoic acid (and less likely to gain visceral fat) whereas the males were still producing the hormone. Examination of fat tissue from these mice led to the conclusion that a sex-specific mechanism allowed the females, but not the males, to use the fat for energy, essentially burning visceral fat. The key to this process involves estrogen. After oophorectomy, the female mice resumed enzyme activity and retinoic acid production, followed by visceral fat accumulation.

The results are applicable to humans because human fat tissue also contains Aldh1a1, and enzyme levels are higher in visceral fat cells from obese than from lean patients. Visceral fat is important because it is linked to obesity, type 2 [diabetes](#), heart disease, and cancer.

The data confirm that genetic factors are an additional cause of obesity and may explain why women gain [abdominal fat](#) more readily than men when eating the same (high-fat) diet. The results also show why postmenopausal women gain weight, given that the protective effects of estrogen are no longer present. The investigators hope that careful modification of Aldh1, perhaps by removing it from visceral fat, will lead to sex-specific treatments for obesity.

Yasmeen R, Reichert B, Deuilis J, et al. Autocrine function of aldehyde dehydrogenase 1 as a determinant of diet- and sex-specific differences in visceral adiposity. *Diabetes*. 2012 Aug 28. [Epub ahead of print]

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