Metformin for diabetes prevention in midlife, obese women

Significant reductions in insulin resistance and body mass index seen after 6 months


**Summary.** Obesity and insulin resistance are associated with the development of type 2 diabetes, and body mass index (BMI) is one of the strongest predictors of progression of prediabetes to type 2 diabetes. Reductions in BMI usually result in reduced rates of progression. Researchers from the Women’s Health Research Program at Monash University in Australia undertook a study to determine whether metformin treatment would affect insulin resistance, BMI, waist circumference, and lipids in 118 obese, but not morbidly obese, euglycemic women (mean age, 53 y) recruited from the community.

Study participants were randomized 1:1 to either metformin or placebo. Treatment with metformin 1,700 mg per day (850 mg twice daily) over 26 weeks resulted in a statistically significant between-group difference in the change in insulin resistance ($P=0.018$) as measured by the homeostasis model of assessment, the primary outcome, over the study period. In addition, statistically significant reductions in BMI ($P<0.001$), HbA1c ($P=0.008$), and fasting insulin ($P=0.03$), and a borderline significant decrease in high-density lipoprotein cholesterol, were seen in the metformin group. No effects were seen on waist circumference, fasting glucose, or other lipids.

**Comment.** In day-to-day practice, we all wish that there was a magic pill to offer our patients for weight loss and to turn back the clock in order to reverse preventable diseases. Midlife and perimenopause are the perfect storm during which time physiology and symptoms clash to rapidly increase the risk of cardiovascular disease, obesity, and diabetes if measures are not taken in a timely fashion. At this crucial time in our patients’ lives, metformin is no magic pill, but it can offer an evidence-based jump start to those motivated for positive change.

As discussed in the NAMS Practice Pearl by Berra and Hughes,1 any effort that we make in the office that engages our patients in positive change and gives them a sense of empowerment over conditions for which they feel powerless can have lifesaving effects. Lifestyle counseling is invaluable, especially when coupled with science-based medical therapy. Although diet and exercise can be as effective as metformin,
this medication can be an especially effective tool for women in the genetic subset of insulin resistance, such as those with polycystic ovary syndrome.

Menopause is a crucial time in our patients’ lives for determining their health trajectory. Davis and associates described weight gain at menopause as especially detrimental to health outcomes, adding to the risks for diabetes and heart disease, and recommend using the last menstrual period as a marker to aid our patients in a process to lose weight and reduce well-known health risks.2

This study by Worsley and colleagues suggests metformin as an insulin resistance-lowering and weight-loss intervention to be used more widely in midlife, overweight women as they face the changes of aging and decreased estrogen levels. Perhaps metformin is another tool to consider in the preventive healthcare of midlife women.

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References

Reduced endometrial cancer risk with use of oral bisphosphonates

Used primarily for prevention and treatment of osteoporosis, the mechanisms for this extra benefit are unclear


Summary. In addition to being a common medication used to treat osteoporosis, bisphosphonates are used to reduce bone metastases in patients with cancer. Its effects on reducing the risk of hormone receptor-positive breast cancer have already been documented, but its relationship with other common cancers is not as well known.

This cohort study of 89,918 postmenopausal women who participated in the Women’s Health Initiative aimed at examining the effects of oral bisphosphonates on endometrial cancer. Detailed health interviews that included history of bisphosphonate use and other regularly used medications were conducted at baseline and throughout the study. At study entry, all women had an intact uterus. Over a follow-up spanning 12.5 years, 1,123 women (1,070 nonusers and 53 users of bisphosphonates) had been diagnosed with invasive endometrial cancer. On evaluation, bisphosphonate use was found to be inversely associated with an age-adjusted, statistically significant (P=.05) reduction in endometrial cancer risk.

Comment. Newcomb and colleagues report a lower risk of endometrial cancer among bisphosphonate users (12 per 10,000 patient-years in nonusers vs 8 per 10,000 patient-years in bisphosphonate users), something that was also found in an Israeli study.1

The biological plausibility for this is not clear to me. Bisphosphonates either bind to bone, where they exert a local action, or are rapidly excreted in the kidneys. Yes, they are used to prevent bone metastases in solid tumors (in 10 times higher doses than what is used to treat osteoporosis), but the benefit there appears to be a direct effect from the presence of the bisphosphonate molecules in bone, especially at the sites of active bone remodeling. How bisphosphonates would get to the endometrium (especially in postmenopausal women, when endometrium is a relatively atrophic and inactive tissue) and what they might do there remains unclear.
With the wide discussion of bisphosphonate-related safety concerns in the lay press (osteonecrosis of the jaw and atypical femur fractures), it’s nice to have some good news. A few years ago, I did a brief literature search that in about 20 minutes turned up 11 observational studies indicating that bisphosphonate users have decreased risks of breast cancer, colon cancer, gastric cancer, stroke, myocardial infarction, and even a lower risk of death.2–11

The main benefits of bisphosphonate therapy are to reduce fracture risk and prevent bone loss. The report of Newcomb and associates does not provide another reason to prescribe drugs from this class, but it adds a little more to the possible “side benefits” of these drugs.

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References

Quality of life for Muslim women living with urinary incontinence

Understanding cultural context and meaning may lead to early diagnosis and intervention


Summary. The purpose of this study by Hamid and colleagues was to help healthcare providers understand the experience of community-dwelling, postmenopausal Muslim women living with urinary incontinence (UI) in Tehran. Seventeen women (age range, 52-68 y) who had experienced UI for more than 10 years were interviewed. Their interviews were analyzed by a phenomenological hermeneutic method, and their experiences were interpreted using three main themes: disruption of normal functioning, self-imposed restriction, and feelings of despair. The researchers concluded that the experience of postmenopausal Muslim women living with UI was destructive in all aspects of their lives.

Comment. Urinary incontinence is one of the most frequent but least acknowledged concerns in women at midlife and beyond. The frequency of UI ranges from 36% in Australia1 to 43% and 57% in the United States.2,3 Risk factors for UI include age, menopause status, parity, obesity, smoking, and hysterectomy.4–6 Although UI is a
concern across all populations, the implications for daily life can be culture specific. The devastating effects of UI in a Muslim community are carefully described in the work of Hamid and colleagues.

Many of the themes and subthemes associated with UI were not surprising (eg, emotional and physical disruptions and self-imposed restrictions), but in the cultural context of Iran, cleanliness is critical to the observance of religious ritual. Women in Tehran described distressing effects of UI on spiritual routines and feelings of despair that went beyond shame and embarrassment. Urinary incontinence made women feel ceremonially unclean, guilty, and sinful, as in being unable to pray, unable to attend religious ceremonies, and unable to make a pilgrimage to Mecca.

Beyond the national boundaries of Iran, this article will be eye opening for any non-Muslim provider who cares for Muslim patients. Urinary incontinence can have culture-specific meanings that patients may not feel comfortable sharing. Hamid and associates make a convincing case for the importance of studying any health-related condition from a cross-cultural perspective. This article provides an accessible, behind-the-scenes glimpse into the meaning and experience of UI among observant Muslim women.

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References

Office-Based Endometrial Polypectomy Can Be Successful

For relieving abnormal uterine bleeding, office polypectomy was noninferior to polypectomy in an operating room, but decisions about treatment setting should be individualized


Summary. Endometrial polyps occur in up to 40% of women with abnormal uterine bleeding and are commonly taken out hysteroscopically. Removing these polyps in an office setting can lower costs and increase convenience because patients can be treated at diagnosis. Investigators in the U.K. conducted a randomized noninferiority trial in >500 women with abnormal uterine bleeding to assess the efficacy and acceptability of office-based versus operating room (OR) polypectomy.

In all, 73% of evaluable women in the office group and 80% in the OR group reported substantial reduction or elimination of bleeding 6 months after surgery, and these effects continued at 12 and 24 months. The efficacy of office polypectomy was at most 18% worse than OR polypectomy (relative risk, 0.9), within the prespecified 25% margin of noninferiority. Partial or failed polypectomy occurred in 19% of the office group and 7% of the OR group.
(RR, 2.5). During the 2-year follow-up, women undergoing office-based polypectomy were twice as likely to undergo at least one more polypectomy and 1.6 times as likely to have additional gynecologic surgery. Treatment was judged unacceptable by 2% of women in each group, and mean pain scores were higher in the office group (although only moderate during the procedure and low thereafter).

**Comment.** The authors note that the decreased costs, absence of general anesthesia, and convenience of office-based polypectomy counterbalance its higher failure rates and pain ratings. While I am encouraged by these findings, I believe the decision to proceed with polypectomy in an office should be individualized. Some women will do well, while others will not—and not all physicians are skilled at this procedure. Other potential impediments include limited insurance reimbursement and difficulties associated with sterilizing instruments in an office setting.

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**Menopause Editor’s picks from April 2015**

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**Hormone therapy and risk of cardiovascular outcomes and mortality in women treated with statins.**  
Ingegärd Anvenden Berglind, MD, PhD; Morten Anderson, MD, PhD; Anna Citarella, PhD; Marie Linder, PhD; Anders Sundström, PhD; and Helle Kieler, MD, PhD.

*Are menopausal hot flashes an evolutionary byproduct of postpartum warming?*  
Lynette Leidy Sievert, PhD, and Allison Masley.

**Use and perceived efficacy of complementary and alternative medicines after discontinuation of hormone therapy: a nested United Kingdom Collaborative Trial of Ovarian Cancer Screening cohort study.**  
Aleksandra Gentry-Maharaj, PhD; Chloe Karpinsky, BSc; Clara Glazer, MD; Matthew Burnell, PhD; Andy Ryan, PhD; Lindsay Fraser, BSc; Anne Lanceley, PhD; Ian Jacobs, FRCOG; Myra S Hunter, PhD; and Usha Menon, FRCOG.
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