

Androgen deficiency in the oophorectomized woman

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Women experience a significant decline in circulating androgen concentrations after bilateral oophorectomy. Despite several limitations, studying women after oophorectomy remains a good model for investigating the effects of both androgen deficiency and androgen replacement. Current data show that most women experience satisfying sexual lives after hysterectomy and bilateral oophorectomy. This is reassuring since elective oophorectomy at the time of hysterectomy is an appropriate option for many women. Oophorectomized women, however, are more likely to report a worsening of sexual function after hysterectomy compared with women who retain their ovaries. Specifically, adverse changes in libido and orgasmic response are more likely in oophorectomized women. After bilateral oophorectomy, women also appear more likely to experience decreased positive psychological well-being. Studies of both the consequences of oophorectomy and the effects of testosterone replacement are consistent with an important role for androgens in female sexual function and psychological well-being. (*Fertil Steril*® 2002;77(Suppl 4):S60–2. ©2002 by American Society for Reproductive Medicine.)

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Women who undergo bilateral oophorectomy experience a dramatic decline in circulating testosterone (T) concentrations. As the postmenopausal ovary continues to be an important source of androgens for women, an approximately 50% reduction in circulating androgen concentrations occurs after oophorectomy in both premenopausal and postmenopausal women. Studying women after oophorectomy, therefore, is a way to evaluate the effects of low androgen levels on libido, psychological state, body composition, bone mineral density, and other factors that may result from decreased androgen concentrations. These women are also excellent subjects in which to evaluate the effects of physiological T replacement on many variables.

There are some limitations, however, to studying androgen deficiency and its consequences in this population. Most women who have their ovaries removed do so for ovarian cancer prophylaxis at the time of hysterectomy. Women who are having oophorectomy for malignant conditions of the ovaries or uterus clearly would not be appropriate candidates for studies of androgen effects on sexuality and other variables. The diagnosis of cancer as well as its subsequent treatment (i.e., surgery, che-

motherapy, and radiation therapy) affects sexuality and psychological state independent of the effects of reduced androgen concentrations. Women whose ovaries are removed for benign conditions such as endometriosis, benign neoplasms, or ovarian cancer prophylaxis in the setting of familial ovarian cancer represent a relatively small number of women. Studies of oophorectomized women therefore are predominantly studies of hysterectomized women as well. As hysterectomy alone may have many effects on sexuality and well-being, studies of oophorectomized women generally need to include women who have had hysterectomies with ovarian preservation as controls. The decision to proceed with elective bilateral salpingo-oophorectomy (BSO) at the time of hysterectomy is a complex and individual one, so women who elect BSO and those who do not may differ in important ways besides resulting androgen concentrations. As it would be unethical to randomize women to BSO or ovarian preservation, there are potential confounding factors inherent in comparisons of these two groups of women.

Simple hysterectomy without oophorectomy may have detrimental effects on sexual function secondary to anatomical changes in

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the vagina and pelvis, although studies typically demonstrate an improvement in sexual function after surgery for benign disease. As women elect hysterectomies for pathology including fibroids, endometriosis, and dysfunctional uterine bleeding, the resolution of dysmenorrhea, pelvic pain, or menorrhagia postoperatively likely results in an improved sexual life. This is consistent with the findings of the Maryland Women's Health Study in which over 1,000 women were interviewed before and after hysterectomy. The investigators observed significant improvements in sexual functioning postoperatively, with increased sexual relations, libido, and orgasms and decreased dyspareunia (1). Studying women after hysterectomy and BSO may overestimate the potential detrimental effects of androgen insufficiency on sexuality if hysterectomy alone worsens sexual function; alternatively, the adverse effects of androgen insufficiency may be underestimated if removal of a uterine pathology alone results in significant improvements in sexual life.

Another limitation of studying the effects of androgen deficiency in oophorectomized women is that estrogen levels also decline significantly with oophorectomy in premenopausal women. Estrogen deficiency results in atrophic vaginal changes and dyspareunia. Ideally, studies of the effects of androgen insufficiency would be performed only in women receiving adequate estrogen replacement therapy (ERT). In studies in which women who have had simple hysterectomies serve as controls, it is important that these women similarly are estrogen replete, secondary to either endogenous or exogenous estrogen. As an additional potential confounding factor, oophorectomized women are more likely to be receiving ERT. Oral ERT dramatically increases circulating concentrations of sex hormone-binding globulin, resulting in even lower concentrations of free T.

Despite these limitations, studies of the effects of oophorectomy on sexual function suggest an important role for androgens. In the Maryland Women's Health Study described above, approximately 44% of the women had concurrent BSO. Although removal of the ovaries did not influence the improvements seen after hysterectomy for measures of frequency of relations, dyspareunia, vaginal dryness, and libido, BSO was associated with a statistically significant 2.7-fold increase in the likelihood of not experiencing orgasms 12 months postoperatively (1). Similar results were found in a retrospective European study. Approximately 700 women under 55 years of age who underwent hysterectomy for benign disease over a 5-year time period at a Swedish hospital completed questionnaires postoperatively. Although most women reported improved sexual life after hysterectomy, oophorectomized women were significantly less likely to report improvement than non-oophorectomized women (55% vs. 74%, respectively) (2). Twenty-four percent of oophorectomized women reported an overall worsening of their sexual life postoperatively, which was more than twice as high as the women who had simple hysterectomy (11%).

Ratings of experience of intercourse and coital frequency postoperatively also were significantly lower in oophorectomized women compared with those who retained their ovaries.

In another retrospective study that controlled for postoperative ERT use, approximately 100 women between the ages of 47 and 55 years who had undergone hysterectomy 2–6 years previously completed the McCoy Sexual Rating Scale, Psychological Well-Being Index, and a semistructured interview. Three age-matched groups were identified: oophorectomized women not receiving ERT, oophorectomized women receiving ERT, and nonoophorectomized women. Overall, there were no differences in frequency of intercourse or orgasm, dyspareunia, arousal, or partner satisfaction between the groups. Women who had their ovaries removed, however, experienced significantly more anxiety and depression, reduced psychological well-being, and lower libido compared with women who retained their ovaries (3).

The impairment of sexual function experienced by some women after oophorectomy appears to affect all aspects of female sexuality. In a study of women who responded to advertisements seeking those with a worsening of their sexual life after hysterectomy and BSO, surgically menopausal women reported a global decline in sexual function. Compared with an age-matched normative population with partners, the surgically menopausal women had significantly reduced sexual thoughts/desires, arousal, frequency of activity, receptivity/initiation, pleasure/orgasm, and relationship satisfaction, with an increase in sexual problems (4).

Although observational studies are informative, an ideal way to assess the importance of a hormone on a variable is to select individuals with the hormone deficiency, restore physiological concentrations of the hormone, and observe the response. As the ovaries are a major source of androgen production for women, oophorectomized women are very good subjects for studies of the effects of androgen replacement. Several studies of supraphysiological T replacement in oophorectomized women demonstrate clear improvements in sexual function. In a prospective, crossover study of 53 surgically menopausal women, those treated with intramuscular T or T-E₂ combined had significant improvements in sexual desire, fantasies, and arousal compared with women treated with E₂ alone or placebo (5).

A study of physiological T replacement in estrogen-replaced surgically menopausal women also demonstrated significant improvements in sexual function. Seventy-five women who experienced impaired sexual function after hysterectomy and oophorectomy were treated with transdermal T (150 or 300 mcg/day) or placebo, each for 12 weeks, in a randomized, double-blind, crossover trial. Despite a considerable placebo response, women receiving the higher T dose experienced significant increases in the frequency of sexual activity and pleasure/orgasm (6). Interestingly, positive well-

being and depressed mood also improved at the higher T dose.

Women experience a significant decline in circulating androgen concentrations at the time of oophorectomy. Despite several limitations, studying women after oophorectomy remains a good model for investigating the effects of both androgen deficiency and androgen replacement. Current data demonstrate that the majority of women experience satisfying sexual lives after hysterectomy and oophorectomy. This is reassuring since elective oophorectomy at the time of hysterectomy is an appropriate option for many women. Ovarian cancer affects approximately 1 in 70 women and is the most common cause of death from gynecologic malignancy. Oophorectomized women, however, are more likely to report a worsening of sexual function, and this information should be discussed with women considering elective oophorectomy. Specifically, adverse changes in libido and orgasmic response are more likely in oophorectomized women compared with those who retain their ovaries.

After oophorectomy, women also appear more likely to experience decreased positive psychological well-being. Studies of both the consequences of oophorectomy and the effects of T replacement are consistent with an important role for androgens in female sexual function and psychological well-being.

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