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INDIVIDUAL SYMPTOMS THAT ARE COMMON TO THE PERIMENOPAUSE AND THE MENOPAUSE

Hot flashes

Estrogen replacement therapy usually relieves hot flashes most effectively. If you start the patient on estrogen and relief does not occur, you need to look for other causes of hot flashes. Thyroid disease would be the most common cause. While checking for hyperthyroidism, also check FSH and estradiol levels. If the latter are within the premenopausal range, it is unlikely that the menopause is the cause.

Occasionally medications can cause sweating and flashes. Obtain a list of the patient's medications, including any herbal preparations that are being used. SSRIs can cause sweating. If a likely drug is found, consider tapering it off and seeing whether the symptoms respond.

In perimenopausal women, there are certain classic triggers. Hot caffeinated beverages, alcohol and hot rooms are the most common ones. Just avoiding these triggers may suffice for control.

If flashes are not severe, consider simple suggestions such as wearing layered clothing (e.g. sleeveless shirt under a sweater).

For symptoms that do not respond to simple relief measures, many patients prefer non-medical interventions, such as vitamins and herbal preparations. When evaluating data on any substances used to relieve hot flashes, you need to look at the placebo arm of the study. Any study without a placebo arm is not reliable. Almost all studies of substances for the relief of hot flashes with a placebo arm will show a reduction in either severity or number of hot flashes of around 40% with placebo. The substance studied must show a significant reduction beyond the placebo arm if it is to be considered efficacious. However, such studies do exist. Almost all studies of non-medicinal therapy are small and time limited. All of this needs to be taken into account when assessing the data.

Soy

Soy and soy derivatives are the most commonly used preparations for relief of hot flashes. Epidemiologically, the country in which women complain least of hot flashes is Japan, which has the highest dietary intake of soy in the world. Soy contains phytoestrogens called isoflavones, notably genistein and daidzein, which have estrogenic activity.

Many alternative medicine experts recommend ingesting full soy products (e.g. tofu, soy milk) for maximum benefit, as epidemiologically mimicking eastern diets (they state that Japanese women eat

whole plant products rather than extracts). However, soy is not a regular component of most western diets, so it is difficult for women in western countries to adapt. Different soy extracts have therefore been used. Most extract products list the isoflavone content. The standard recommendation is 45-60 mg of isoflavones daily for relief of symptoms. Preparations that are available in the USA include Healthy Woman, Estroven and Revival Soy.

The most controversial risk of soy is its effect on the breast. Most studies show beneficial or neutral effects on the breast. Many experts believe that soy acts as a selective estrogen receptor modulator (SERM), producing an estrogenic effect in some tissues and blocking estrogenic activity in others (namely the breast). Many point to the fact that Japanese women living in Japan have among the lowest breast cancer rates in the world, partially due to their high soy intake. (However, some believe that it is exposure to soy during the teenage years, when breast tissue differentiation actively occurs, as opposed to exposure later on in life, that is beneficial.)

Black cohosh

Although it is not a phytoestrogen, in some studies black cohosh seems to show efficacy in the therapy of hot flashes. Very limited studies have been conducted in the USA, and the majority of data on cohosh come from Germany. German authors recommend its use for a 6-month period, and then recommend re-evaluation to ascertain whether it is needed any longer.

Some experts in the USA are skeptical about the benefits of cohosh, but few have noted any significant hazards. Because it is not a phytoestrogen, it steers clear of the breast cancer controversy. Nonetheless, we do recommend that our breast cancer patients discuss it with their oncologists. Common preparations available in the USA include Remifemin® and Estroven®.

Medical approaches

Selective serotonin reuptake inhibitor/Selective norepinephrine reuptake inhibitor (SNRI) therapy: Although occasionally associated with the side-effect of sweating, most SSRIs and Effexor (venlafaxine, the main SNRI) have been studied with success with regard to the suppression of hot flashes. Standard low-dose antidepressant dosages are used. If the patient is also suffering from depressive symptoms, this may be an ideal approach to both problems.

The two main concerns we have with regard to the use of certain SSRIs in perimenopausal women are weight gain and decreased libido. The side-effect of weight gain is most commonly seen with Paxil® (paroxetine). Most perimenopausal women complain of unwanted weight gain, and if they feel that their medication is further adding to their problem, they will not want the therapy.

The other concern is decreased libido. Many perimenopausal women complain of lack of libido, and a well known side-effect of SSRIs is potential loss of libido. If a significant loss of libido is a chief complaint as well, we would avoid SSRI therapy.

Insomnia

We ask every patient in her forties at her annual visit what her sleeping is like. The most common answer we receive is “Terrible - but why do you care? You are my gynecologist”. Many perimenopausal women have sleep disturbances, but do not associate these with hormonal changes.

The classic perimenopausal sleep pattern is that a woman will fall asleep readily and early, as she is exhausted. She then wakes up at 1 or 2 a.m., cannot fall asleep again for 1 or 2 h, finally falls asleep at 4 a.m., and then wakes up to go to work at 6 a.m., after which she is fatigued all day. This pattern can normally be readily differentiated from a depressive insomnia, which is usually associated with difficulty falling asleep and with earlymorning wakening.

Sometimes this sleep disruption will be accompanied by hot flashes, while at other times the woman will just awaken spontaneously. Some sleep research has shown that even in women who do not report insomnia, the quality of menopausal sleep is poorer.

Again HRT is usually successful. For the patient who does not want HRT, there are other options. One variant of HRT can be helpful. For decades, natural progesterone has been known to cause somnolence (many years ago anesthesiologists used it as an adjunct for sedating their patients). Therefore if a woman is willing to take natural progesterone before sleep, this may help. If the woman wants a commercially available natural progesterone, Prometrium is available with a prescription.

Lifestyle changes

The more active a woman is during the day, the better she will sleep at night. However, you should encourage her to exercise early in the day (or at least before dinner), because evening exercise may make it more difficult for her to fall asleep.

Alcohol use

Perimenopausal women are at high risk of becoming dependent on alcohol, and one of the problems that can drive them that way is sleep disruption. Question your patient about her alcohol use, if you have any prompts which lead you in that direction, and offer to help her to solve her sleep problem without developing a reliance on alcohol.

Vaginal dryness

Unlike hot flashes, which tend to get better over time, the progressive loss of estrogen through the peri- and postmenopause unfortunately tends to cause increasing problems with vaginal atrophy. Not all women are bothered by atrophy. Of course, overweight women will have peripheral production of estrogen, which may be sufficient to maintain vaginal lubrication. Usage of the vagina by regular sexual activity does tend to promote more pelvic blood flow, so the old adage (which your patients have heard) `Use it or lose it` does have some truth to it.

For many women, the vaginal dryness is only an issue when they have intercourse, and they will find

that a short-acting lubricant, available over the counter, is all they need. Common brands are K-Y Jelly® and Astroglide®. Discourage your patient from trying the old remedy Vaseline, because it seldom provides appropriate lubrication.

However, for many women the atrophic changes are more bothersome. They may experience recurrent vaginitis, or they may find that a simple lubricant does not help their painful intercourse. As more women are stopping their systemic HRT (or not initiating it in the first place), atrophic complaints are becoming more prevalent. And because many women are reluctant to complain of vaginal discomfort, during your annual examination of your postmenopausal patient you should specifically ask her about vaginal comfort.

Fortunately, atrophic vaginitis is fairly straightforward to treat, and multiple products are now available for therapy. The traditional standard therapies are vaginal estrogen creams. A variety of products are available, notably estradiol (Estrace) and conjugated equine estrogens (Premarin) creams. These are prescription drugs which are sold in a tube with an applicator. Woman can use 1 to 2 g of the preparation, which they place intravaginally before bedtime. Most women end up using an application two to three times per week. We encourage our patients to adjust use of the cream according to their symptomatology.

There is systemic absorption from vaginal creams, but it is relatively minor. Because endometrial hyperplasia is not seen with cream use, most gynecologists do not recommend systemic progestin withdrawal concomitant with vaginal estrogen use. Some conservative gynecologists will ask their patients to withdraw to progestins every 3 or 4 months if they are using a vaginal cream frequently. Because of the systemic absorption, some oncologists will not allow their breast cancer patients to use vaginal estrogens. This is obviously a major problem. If a young woman with breast cancer has to undergo chemotherapy, her ovaries usually cease to function, at least temporarily. These women will usually have significant atrophic symptoms, making them even more uncomfortable. The pros and cons of the therapy should therefore be considered.

More recently, a product called the Estring® has become available. This is a silicone ring which can be described to your patients as looking similar to the ring of a small contraceptive diaphragm, without the cup. It is combined with estradiol, and provides a chronic slow release of estrogen to the vaginal mucosa. The ring does elevate systemic estradiol levels for the first day that it is placed. However, shortly thereafter the blood estradiol levels fall significantly, basically back to the pre-insertion range. The ring can remain in place for 3 months, and the patient can then change it herself (or if she is unable to do so, her partner can be shown how to do this, or the occasional patient will need to have it changed by her healthcare provider). The ring is fairly unobtrusive (our patients and their partners say that they cannot feel it). Many oncologists are happier with the ring as a vaginal estrogen delivery system, because of the lower systemic levels that are reported.

Vagifem® vaginal tablets are small tablets of estradiol which can be placed vaginally to relieve atrophic symptoms. They are supplied with a vaginal applicator which is used to place the tablet high up in the

vaginal vault. These tablets should be placed before bedtime, and will then dissolve. As with creams, you should explain that these products are not lubricants for intercourse, and that they should be used on a non-intercourse night. Of course, women who still require extra lubrication can use K-Y jelly or Astroglide as well.

Vagifem tablets seem to give less elevation of the serum estradiol levels, and may therefore also be preferable to creams for breast cancer patients. However, most of the time use of the various products will really depend on patient preference. For some women, the Estring is excellent, because they then only have to think about vaginal therapy once every 3 months. However, some women feel anxious about anything remaining in their body, and prefer a therapy that can be inserted on an `as-needed` basis.

Some women prefer the feel of the vaginal creams, whereas other women find them messy and prefer the vaginal tablets, which tend to 'drip' less. Some women have atrophic symptoms of the vulva, and for these patients the cream is needed for their external anatomy. Other women will use the tablets in the vagina, and apply creams externally.

Unfortunately, these products are relatively expensive. We encourage our patients to shop around at different pharmacies and pharmacy services to find the least expensive location.

Of course, as with all estrogenic substances, some patients are unwilling even to consider any vaginal estrogens. For these women, long-acting vaginal lubricants (e.g. Replens®) are available which are placed into the vagina several times a week for relief of atrophic symptoms.

Some botanical lubricants are available. In Europe, a preparation called Phyto Soya® vaginal cream is available and is quite popular, but this particular preparation is unavailable in the USA at present. Other botanical lubricants are available and may be helpful. The vaginal mucosa is of course among the most sensitive tissues in the body, and therefore any substance can irritate it (some women are sensitive to the base in which the Estrace and Premarin products are dissolved). Therefore if your patient's vaginal complaints seem to be getting worse, not better, consider the possibility of skin irritation, and suggest an alternative product.

There is no contraindication to the concomitant use of SERMs and vaginal estrogens, so if your patient is taking raloxifene for protection against osteoporosis, there is no reason why she cannot use vaginal estrogen preparations to relieve atrophic symptoms.

Urinary symptoms

Many perimenopausal women complain for the first time in their lives of bladder problems. They may experience urinary tract infections or incontinence. Often they will end up being referred to a urologist, and they will undergo a significant work-up for a problem that could be easy to treat, as some urologists do not consider the possibility of menopausally related issues causing bladder problems.

For almost any urinary symptom, you should always start with a urinalysis and urine culture. Diabetes is now appearing in our population in epidemic proportions, and a urinalysis showing glycosuria requires further work-up. An infection in any woman requires therapy, and ideally a follow-up culture to make sure that her bacteriuria has cleared.

You should then inquire about any vaginal atrophic symptoms and perform a pelvic examination. We explain to our patients that their bladder arises embryologically from the same tissue as does their vagina, and that it possesses similar estrogen receptors. Therefore it is not surprising that women can present with symptoms related to bladder atrophic changes. In a woman with recurrent urinary tract infections, a dose of vaginal estrogens (see above) once or twice a week may be all that she requires to prevent further infections. Some women will experience urinary symptoms such as frequency, urgency and nocturia, even without infections, just related to atrophic symptoms. Vaginal estrogens, because of their absorption to the neighboring bladder, may resolve these symptoms for the patient. Of course, if she has other indications for systemic HRT, the latter should also resolve her bladder symptoms.

Incontinence is a more complicated phenomenon. Any woman who presents with leakage of urine needs to have a good history taken. Does leakage occur on coughing, sneezing or exercise? This is more commonly seen with anatomic stress incontinence. Does the woman feel that she has to get to the bathroom in a hurry? Does she leak whenever she thinks about urinating? Does she feel the need to urinate frequently? These symptoms are more common with so-called urge incontinence, or detrusor dyssynergia. Many women present with a mixed picture.

Concomitantly, all women should be encouraged to do Kegel's exercises (squeezing of the pelvic floor muscles). Although these exercises were originally thought to help only anatomic stress incontinence, recent studies have shown that women with urge incontinence may also benefit from them. You can check your patient during her pelvic examination to see whether she is doing her exercises correctly (simply ask the patient to contract her vaginal muscles around your fingers during a digital examination).

Encourage your patient to do as many Kegel's exercises as she can during the day. We encourage our patients to put a sign on the dashboard of their car, to remind them to do Kegel's while they are stopped at stoplights, or in traffic. Another time they could do them is while pumping gas.

Many physical therapists are now trained in pelvic floor exercises. You can refer your patient to such a therapist, who may be able to improve your patient's techniques and her pelvic floor strength. Most physical therapists will incorporate biofeedback techniques as well.

Weight is also a major factor here. Weight loss will almost always improve incontinence. Of course, if a patient is contemplating any surgical procedure for incontinence, one of the major causes of surgical failure is obesity. Therefore weight loss will either remove the patient's need for surgical intervention or, if she still requires surgery, it will significantly improve the chances of success.

For the patient for whom weight loss, Kegel's exercises and estrogen therapy have failed, other pharmacological interventions for incontinence are available. For the patient with urge incontinence, the old standard therapy was oxybutinin (Ditropan®). The actions of oxybutinin are anticholinergic, and although it often worked well for urge incontinence, the side-effects of dry mouth and constipation were often more unpleasant for the patient than the incontinence. However, a newer extended-release product is available, and with this XL product, the side-effects have been reduced.

Tolterodine (Detrol®) was developed more recently. Its activity is also anticholinergic, but it has less of a dry-mouth effect. It is also available in a longacting form. The major contraindication of Ditropan and Detrol is uncontrolled narrow-angle glaucoma. These drugs will act fairly quickly, so that in a matter of a few days to weeks your patients' responses can be clearly seen.

Although the approach to urge incontinence is primarily pharmacological, the approach to stress incontinence has traditionally been surgical or mechanical (in the form of pessaries). Pessaries have been available for many years. Many younger practitioners have never seen a pessary. This is a rubber or plastic gadget which is available in many shapes, from rings to cubes to dishes, which are designed to fit in the vagina and support the pelvic floor, and by exerting pressure on the urethra to stop leakage of urine. Many women are quite comfortable using them and become adept at inserting and removing them themselves. For the woman who does not wish to undergo surgery, pessaries may be an ideal solution. For women who develop mild incontinence, particularly with exercise, insertion of a vaginal tampon prior to exercise may relieve their symptoms.

For women who are extremely poor surgical candidates, pessaries can also be very useful. These women, who are often elderly and have significant prolapse as well as incontinence, will usually be unable to remove these pessaries on their own, and will require a check-up by the practitioner every 3 or 4 months to remove the pessary and cleanse the vagina.

For younger women with true stress incontinence for whom more conservative therapy has failed, surgical intervention can be quite helpful. Traditional bladder suspension procedures have been performed for many years. Many urogynecologists are now using the tension-free vaginal tapes to suspend the bladder and urethra. The advantages of this procedure are that it is performed on an outpatient basis, with relatively quick recuperation. The initial success data are good, but obviously long-term data are not yet available.

Again, as many women are embarrassed about discussing incontinence, if you feel that this is an issue for your patient, raise it with her, and reassure her that this is an extremely common problem. Encourage her to think about interventions.