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REVIEW ARTICLE

Managing Vasomotor Symptoms in Menopausal Women

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ABSTRACT

Patients usually under-report symptoms of incontinence. Therefore, improved physician-patient communication is vital. Most urinary incontinence can be evaluated and treated after careful history and simple clinical assessment. Initial treatment, for both urge urinary incontinence and stress urinary incontinence, is lifestyle modification and pelvic floor muscle exercises. Urgency responds to bladder training and drug therapy with anticholinergic medication. Pharmacotherapy has a limited place in stress incontinence.

Keywords: Urinary incontinence, Overactive bladder, Anticholinergic drugs.

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The symptoms of vasomotor instability associated with menopause are called hot flashes. Hot flushes are recurrent, transient episodes of flushing, perspiration and a sensation ranging from warmth to intense heat on the upper body and face and may be sometimes followed by chills. Most hot flushes stop over time without therapy. Incidence of hot flashes increases during peri-menopause, reaching its highest rate during the first 2 years post menopause and declining over time consistent pattern of hot flashes in within a woman and a circadian rhythm has been observed. Though Indian data is lacking, according to Western data, hot flushes are experienced by 10 to 83% of women. After surgical menopause hot flush rate of up to 90% have been reported. But with passage of time symptom rate, become similar to women with naturally acquired menopause.[1]

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Various factors seem to be related to hot flash frequency:

1. Warm temperatures increase a women's core body temperature and makes her more likely to reach the sweating threshold. Cooler air temperatures are associated with a lower incidence of hot flashes.
2. In perimenopausal women, a high BMI (> 30 kg/m^2) is associated with an increased risk for hot flashes as compared to women with low BMI (> 24.9 kg/m^2). But in postmenopausal women this association is not found.[2]
3. Cigarette smoking (past and current) is associated is with an increased relative risk of hot flashes.[3]
4. Strenuous exercise may trigger hot flashes, low ever daily exercise is associated with an overall decreased incidence.
5. Women who have less physical activity have an increased relative risk of hot flashes.
6. Women of low socioeconomic status have an increased relative risk of hot flashes.
7. There is no significant association between alcohol intake and hot flashes rate.
8. There is no evidence supporting relationship of hot flashes with emotional stress and consumption of caffeine, hot or spicy food.

ETIOLOGICAL CONSIDERATIONS

Although, the exact etiology of hot flashes is not known. A hypothalamic origin has been suggested.

Endocrinology

An acute decrease in the level of estrogens plays a role in the genesis of hot flashes rather than low levels *per se* and an acute increase in lutenizing hormone levels has been refuted as a cause for hot flashes. No casual relationship has been associated between opiodergic system and hot flashes.[3]

Thermoregulation

Elevated brain nor epinephrine levels narrows the thermoregulatory zone in symptomatic women and small elevations on core body temperature triggers hot flashes when sweating threshold is crossed.[5]

Recommendations for Management of Vasomotor Symptoms

Treatment of vasomotor symptoms due to menopause is a common clinical challenge. Before starting treatment, a detailed history of woman regarding frequency and severity of hot flashes and their effect on patients daily activities should be enquired.

No treatment is required unless hot flushes are bothersome to the patient and disrupts her day to day activities. Therapy should be tailored to each woman's needs. The decision to start treatment should be based on the severity of symptoms individual woman's attitude toward menopause and medication and assessment of risks related to treatment.

There is a tendency of natural regression of symptoms over time in most women. In majority of women treatment for hot flashes can be discontinued within a year.

Since, obesity and sedentary lifestyle are related to hot flushes patient should be advised to maintain a healthy weight and to do regular exercise. Use of fans, air conditioners and light cotton clothing may be helpful.[6,7]

1. For mild vasomotor symptoms, the first strategy should be life style changes be life style changes like regular exercise, keeping the core body temperature cool and paced respiration (Slow Controlled diaphragmatic breathing).[7-9]
2. When the desired relief from hot fishes is not achieved addition of nonprescription remedies maybe considered, as these are comparatively free of side effects. Vitamin E, 800 IU/day is nontoxic at this doses, inexpensive and can be tried for relief of hot flushes. Use of evening primrose oil and Ginseng is not superior to placebo. When therapy is required various nonpharmacologic and pharmacologic options are available.[10]
3. For women who cannot or do not wish to use estrogen for control of server vasomotor symptoms, life style modification should be the first step.[11,12]
4. If drug therapy is required the most effected non-estrogen class of agents is antidepressants Venlafaxine is the most beneficial in this class.[13]
5. If antidepressants are not tolerated clonidine may be tried.[14]
6. Gabapentin in a promising new therapeutic options (long term efficacy and safety remain to be substantiated).
7. Soy may have some estrogen agonist activity. A healthy diet incorporating soy protein seems reasonable (Grade C). Women should be encouraged to use whole food sources, rather than supplements, because of the risk of overdosage and lack of known long-term effects of soy supplements. The adverse effects reported red clover is oflavones seem minimal, although the long-term safety of red clover has not been confirmed.[10]

Nonhormonal Therapy for Management of Vasomotor Symptoms

Data regarding the estrogenic effects of soy are inconclusive.

Clinical trial are insufficient to support or refute efficacy of soy foods and iso flavones supplements (soy or red clover) i.e. Phytoestrogens, black cohosh, vitamin E, dong quai, evening primrose oil, ginseng, acupuncture or magnet therapy [Level of evidence (LOE)].[2]

Women with a personal or strong family history of hormone dependent cancers (breast, ovarian or uterine), thromboembolic events or cardiovascular events should not use soy based therapies (grade-D).

Clinical trial have not been conducted on use of licorice for hot flushes.

WHEN TO START HORMONE THERAPY HT?[12]

No therapy other than estrogen has been approved by FDA for treatment of vasomotor symptoms.

For patients with persistent and severe hot and flushes hormonal therapy is the option (LQE 1, grade A)

HT is the most effective intervention for menopausal hot flushes.

HT should be used for the shortest duration of time necessary to control symptoms at the lowest dose.

HT is prescribed during the perimenopause for relief of menopausal symptoms (LOE 1, grade A).

The short-term use (5 years or less) of estrogen and progestin does not seem to be associated with significant risk (grade B). Estradiol is the first-lime estrogen (orally or transdermally) (grade C).

In a cyclic regimen-progestational agent should be added for 10 to 14 days in women with intact uterus (LOE-1, grade A).

With advancing age, the dose may be reduced (grade C).

Use of progestegen for 14 days every 3 months has not been validated for effectiveness, but it has been proposed to reduce exposure of breast tisane to progestogen (grade B).

Only very small percentage of women continue to suffer from hot flushes 10 years after the onset of menopause therefore longer HT may be appropriate in these women depending on the benefit *vs* risk profile (grade C).

Treatment should be periodically evaluated to determine if it is still necessary, as in almost all women, menopause related vasomotor symptoms will abate over time without any intervention.

CONTRAINDICATIONS TO HT

1. Current, past or suspected breast cancer.
2. Known or suspected estrogen-sensitive malignant conditions.
3. Undiagnosed genital bleeding.
4. Untreated endometrial hyperplasia.
5. Previous idiopathic or current venous thromboembolism (deep vein thrombosis, pulmonary embolism).
6. Active or recent arterial thromboembolic disease (angina, MI).
7. Untreated hypertension.
8. Active liver disease.
9. Known hypersensitivity to the active substances of HT or to any o the excipients.
10. Porphyria cutanea tarda (absolute contraindication)

Most commonly used preparations are:

- Conjugated equine estrogen (0.3-0.625 mg) with Medroxyprogesterone acetate 2.5 per day
- Micronized 17 β estradiol (0.5-1 mg)
- Ethinyl estradiol (0.01-0.02 mg)
- Transdermal estradiol (14-100) microgram and vaginal estrogens.

Use of androgens in women for any use has not been approved by FDA 12).

Primary indication for systemic ET and EPT is treatment of moderate to severe menopausal symptoms.

While prescribing HT its contraindications and adverse effects should be kept in mind.

Progestogen

The primary indication for their use is for endometrial protection from unopposed ET.

Use of progestogen contributes substantially to increased breast cancer risk.

Commonly used oral progestational agents are MPA, norethindrone, LNG, micronized progesterone.

Intramuscularly medroxyprogesterone acetate (MDA) 150/mg 1 month in depot form in effective therapy for hot flushes.

Oral progesterones shown to have endometrial protection (LOE1).

- Medroxyprogesterone acetate (MPA) (2.5 mg daily or 5 mg for 10 to 12 days/mo).
- Micronized progesterone (100 mg daily or 200 mg for 10 to 12 days/mo).
- Norethindrone (0.35 mg daily or 5 mg for 10 to 12 days/mo).
- Levonorgestrel (0.075 mg daily).

Even lower than standard doses of ET and EPT (daily 0.3 mg conjugated estrogen, 0.25 to 0.05 mg 17β estradiol, 0.025 mg 17β estradiol) provides similar relief from vasomotor symptoms.

If initial ET/EPT dose is not effective, it may be increased.

In women who do not get relief from vasomotor symptom from oral therapy may be switched over to transdermal therapy. Another option is the use vaginal estrogen ring.

Continuous ET is recommended over cyclic therapy since in the cyclic therapy, hot flushes may return by the end or hormone free week.

If vasomotor symptoms persist after 2 to 3 months of therapy, others differential diagnosis should be considered.

On discontinuation of HT abruptly, hot flushes often return within days. So gradual reduction in dose is recommended for avoiding rebound hot flushes or the time between the doses may be increased.

Progestogen alone can be used to treat hot flushes. DMPA, MPA and megesterol acetate are efficacious.

In perimenopausal women who require contraception along with relief of vasomotor symptoms may benefit from low dose combined oral contraceptives (OCs). But if EPT is required postmenopausally also, as soon as possible OCs should be switched over to EPT.

Nonhormonal Options

In women with vasomotor symptoms for women hormones are not an option other drug therapy is available.

Clonidine, antidepressants venlafaxine, paroxetine and fluoxetine and the anticonvulsant gabapentin have demonstrated some efficacy for treating hot flushes (LOE2).

Venlafaxine (Doses used to treat depression start at 75 mg/day and increase to 150-225 mg/day).

Side effects of these agents may include nausea, dry mouth, insomnia, fatigue, sexual dysfunction and gastrointestinal disturbances.

Fluoxetine (20 mg/day), paroxetine (12.5 or 25 mg/day) for 6 weeks.

Gabapentine (900 mg/day) side-effects may include fatigue, dizziness and peripheral edema.

Antihypertensives[15]

Cloridine (0.1 mg/day) side effects, including dry month, postural hypotension, fatigue and constipation, often limit the use of this medication.

Methyldopa (500-1000 mg/day) causes significant reduction in hot flushes.

CONCLUSION

Hot flashes can be very distressing symptom in perimenopausal women, assurance and nonpharmacological options need to be tried first and if not relieved drugs to be used. Usually drug therapy is required for not more than 1 year.

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