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Hormone replacement therapy and sexuality

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Introduction

Menopause is a major turning point in women's sexuality. Observational studies indicate that sexual inactivity triples in women from 50 to 60 years of age in comparison with the male partner of the same age cohort, reflecting a major sexual crisis among couples in this age group [1]. Women's sexuality is multifactorial, rooted in biological, psychosexual and context-related factors, and is multisystemic: a physiological response requires the integrity of the hormonal, vascular, nervous, muscular, connective and immune systems [2]. Because of this solid biological basis, women's sexuality may be affected by the loss of sexual hormones; the younger the woman, the stronger the negative effect [3–5].

Female sexual problems are age-related, progressive and highly prevalent, affecting up to 43% of women [1]. A third to half of women regard the problem as distressful [6]. Sexual disorders have been associated with poor quality of life, lower perception of well-being, lower self-esteem, poor self-image, poor relationship quality, depression and anxiety [3, 4].

Sexual problems increase with age [1]. The menopause has a further detrimental effect [4, 6]. Estrogen and progesterone production stops with ovarian exhaustion. Testosterone production gradually reduces from the twenties onwards but is maintained across the natural menopause. It is completely lost after bilateral oophorectomy [7].

Severity of sexual impairment varies according to:
— age at menopause (the younger the woman the higher the vulnerability) [5, 6];
— its etiology (spontaneous or iatrogenic, from benign or malignant conditions) [5];
— the woman's general health status and lifestyle [2, 5, 7];
— the quality of medical care [5].

Predisposing, precipitating and maintaining factors, both biological and psychosocial, contribute to the pathophysiology of female sexual disorders during the menopausal transition [8]. Sexual symptoms and signs of menopause can be attenuated by the possibility, availability and feasibility of hormone replacement therapy (HRT) [9–11].

Indications for HRT and sexual benefits

Menopausal sexual symptoms

Observational studies have linked the menopause-related decline in estradiol to a decline in sexual interest, enjoyment, arousal and orgasm [4, 6]. The direction of causality is that the decline in estradiol increases vasomotor symptoms, which affect mood, which then affects sexual response [4]. Sexual symptoms, when caused by a domino negative effect due to menopausal autonomic disruption and loss of genital trophism, can be relieved by HRT [9–13]. Progestogens, according to their structure, metabolic and endocrine profile [5, 7, 8] can potentiate or oppose the positive action of estrogens on sexuality [10].

"Decline in estradiol increases vasomotor symptoms, which affect mood, which then affects sexual response."

Premature menopause

Women undergoing premature menopause (either due to premature ovarian failure or to iatrogenic causes) are more exposed to the long-term consequences of sexual hormone deprivation: the earlier the menopause, the worse the impact on a woman's general health and sexual well-being [6, 12]. This neglected group of patients is increasing (reviewed in [12]). Spontaneous ovarian failure affects on average 1% of women under 40 years of age [14]. Iatrogenic menopause, for benign and malignant conditions, affects 3.4–4.5% of women under 40 [12, 15, 16] and up to 15% between 40 and 45 years of age. The 5-year survival for all malignancies in childhood and adolescence is 72% (up to 90% for some cancers) [17, 18], with an increasing number of survivors facing the challenges of adulthood deprived of their gonadal hormones unless appropriate HRT is prescribed. Distressing sexual disorders are more frequently reported in women with premature menopause [4, 6, 12], particularly after bilateral oophorectomy [4, 6]. In women with premature menopause, the risk of breast cancer after HRT corresponds to that found in premenopausal women of similar age who have not suffered an iatrogenic or premature menopause. It is recommended that women who have undergone premature menopause (unless associated with hormone-dependent cancer, such as breast cancer or genital adenocarcinoma) should be offered HRT, at least until the average age of menopause (51 years) [9–11].

"Women who have undergone premature menopause (unless associated with hormone-dependent cancer, such as breast cancer or genital adenocarcinoma) should be offered HRT, at least until the average age of menopause (51 years)."

Urogenital and sexual symptoms

Atrophic changes in the urogenital tract and their consequences (e.g. vaginal dryness, dyspareunia, urinary frequency and urgency, postcoital cystitis) are improved by estrogen therapy. When prescribed solely for the treatment of such symptoms, topical low-dose vaginal products are the treatment of choice [2, 9–13]. Estrogen therapy may well address the urogenital comorbidity that increases with increasing age [13] unless appropriate estrogen therapy is prescribed. Long-term treatment is often required, as symptoms can recur on cessation of therapy [7, 9–11, 13].

Other benefits

HRT can slow the typical thinning of the skin and the mucosal atrophy that occurs after menopause. The positive impact on skin, mucosal appearance and trophism can greatly improve personal confidence, self-image and feelings of well-being [2, 12].

Drugs of choice to improve sexuality

Androgens

Randomized controlled trials indicate the positive effect of testosterone in estrogen-treated women on different domains of female sexual function (reviewed in [3, 4, 19]). The use of androgens locally for vulvar dystrophy and clitoral insensitivity is often overlooked, but androgens are a very efficacious treatment for genital sexual dysfunction [2]. Dehydroepiandrosterone administration can improve quality of life in elderly patients. A recently published randomized placebo-controlled trial was conducted in surgically menopausal women (aged 24–70) who developed stressful hypoactive sexual desire disorder [20]. Treatment with 300 μg/day testosterone patches on estrogen-treated women increased sexual desire, frequency of satisfying sexual activity, arousal and orgasm, while decreasing distress and concerns. It was well tolerated [20]. However, this treatment is not approved at the time of writing (July 2006).

Tibolone

Tibolone is a prodrug which after ingestion converts to various metabolites that are systemically active as progestogen, androgen or estrogen. It has different actions on different target organs, which provide an overall favourable risk-benefit profile [2, 12, 13, 21]. Clinically, tibolone treats menopausal symptoms, including hot flushes and vaginal dryness, as effectively as estrogen therapy, and, most importantly, improves sexual response, while having a positive effect on bone [21].

"The use of androgens is often overlooked, but androgens are a very efficacious treatment for genital sexual dysfunction."

Progestogens with androgenic activity

Norethisterone acetate, and other 19-nor-derivatives that have agonist activity on the androgenic receptors, may potentiate the effect of estradiol in improving sexual function in postmenopausal women [13].

Conclusion

In view of the current level of evidence, HRT should be prescribed when it is clearly indicated for menopausal symptom relief, including relief of sexual symptoms. There is no effective alternative to estrogen or estrogen-progestogen treatment, with testosterone providing an added bonus to sexuality. HRT has a specific role in women with premature menopause, who comprise the group most distressed by their sexual symptoms. Treatment should be considered until the age of natural menopause (51 years), unless specific contraindications exist. The need to continue with treatment and the presence of indications for HRT should be reviewed regularly when used in the long term. Constant updating is required in the rapidly evolving field of menopausal management.

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