2. PERIMENOPAUSAL WOMEN

DEFINITION

The perimenopausal phase begins with the symptoms of the approaching menopause and ends 12 months after the last menstrual period. Cessation of menstruation is not always helpful as a basis for management since amenorrhoea is often preceded by manyyears of oestrogen-dependent symptoms.

From a biological viewpoint, ovarian function declines gradually, with the cessation of periods as the end point. The transition from reproductive to non-reproductive state is referred to as the climacteric and may last for more than 10 years. This is marked by irregular periods, decreasing fertility, increasing premenstrual syndrome and climacteric depression.

DIAGNOSIS

The diagnosis is often a difficult one to make as symptoms will commonly coexist with regular menses. See Card 1, Table 1 forcommon symptoms.

Assays of oestradiol, FSH and LH (most diagnostic in the early follicu lar phase) may be unreliable as these represent merely a snapshot of the hormone profile of the individual at that particular time and levels mayfluctuate on a daily basis'.

TREATMENT OF THE PERIMENOPAUSAL WOMAN WITH HRT

Treatment may need to be given empirically if the diagnosis is uncertain, and appropriateness of treatment gauged by the response of the individual. Advice should be given as to the advantages and disadvantages of each route of administration, but ultimatelythe woman's choice is of paramount importance as this is what will ensure adherence to therapy. Oestrogen only HRT should be prescribed in the hysterectomised woman.

SEQUENTIAL HRT

In orderto minimise the risk of breakthrough bleeding (BTB) treatment should be:

- commenced with sequential HRT;
- timed to the endogenous cycle (if still discernable);
- and commenced on day one ortwo of menstruation (if still menstruating).

SWITCH TO CONTINUOUS COMBINED HRT (ccHRT)

It can be difficultto know exactly when to switch treatment from sequential to continuous combined therapy. Many datasheets still advise that continuous combined therapy is not commenced before the age of 54 years (the age when 80 per cent of women will be postmenopausal) or after 1 year of sequential therapy. However, there are some data that support the use of ccH RT in the late perimenopausea.

Data suggest that the risk of endometrial hyperplasia is higher with sequential therapy'. Other data also suggest that despite the addition of cyclical progestogen the risk of endometrial carcinoma is not eliminated'. In view of this, ccHRTshould be commenced immediately if a woman is postmenopausal (>_1 year amenorrhoea, even if she is less than 54 years) or 1 year after commencing sequential HRT.

Women should be advised that BTB may occur in the first 6 months of therapy. **Allowing a gap of 2to 3 weeks between the sequential and ccHRT may reduce BTB by allowing the endometrium to shed prior to the switch.**

OTHER REGIMENS FOR THE PERIMENOPAUSE

Long cycle HRT reduces the number of progestogenic episodes and withdrawal bleeds to four peryear. However, data suggest an unacceptably high incidence of endometrial hyperplasia and bleeding problems due to the prolonged episodes of unopposed oestrogen.

An intrauterine system is soon to be licensed inthe UK to provide continuous progestogenic opposition foroestrogen therapy and therefore endometrial protection. This will be ideal for perimenopausal women providing contraception, ccHRT in the perimenopause and high rates of amenorrhoeas.

ORAL HRT

HRT in tablet form is the most popular form of treatment, is cheap and convenient and raises H DL levels. Disadvantages are:

- 60 percent of the absorbed dose is converted to oestrone bythefirst-pass livereffect.
- 2:1 ratio of oestradiol:oestrone (less potent) in premenopausal women is reversed.
- An increase in hepatic proteins occurs.

There are various forms of oral sequential HRT available for perimenopausal women. Androgenic progestogens give good cycle control. In standard or high dose preparations, less androgenic progestogens may give less progestogenic side effects. However, low dose preparations containing androgenic progestogens, eg norethisterone, have been shown not to cause progestogenic side effects.

Recent developments indicate that initiation doses of HRT can be lower than was originally thought leg 1 ratherthan 2mg of oestradiol). The benefits of symptom relief and osteoporosis prophylaxis are maintained whilst side effects are minimised [2A].

NON-ORAL HRT

There are now numerous ways in which HRT can be administered systemically in a non-oral form: patches, gels, nasal, vaginal and implant. At present, combined non-oral HRT is only available in a patch where 1 7f3 oestradiol is combined with either norethisteroneor levonorgestrel forthe last 2 weeks of the 4-week cycle.

Advantages

- Avoidance of first pass metabolic effects.
- Oestrone:oestradiol ratio is maintained within premenopausal levels.
- No significant changes occur in the concentration of hepatic proteins.

Disadvantages

- Typically more expensive than oral therapy.
- No beneficial effect on HDL'.
- Less effective endometrial transformation bytransdermal progestogens.

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