Diagnosis and management of menopause

Dr Sarah Gray presents the management pathway for menopause

Recognition

Bleeding pattern progressively changes:
1 Cycle shortening with or without exacerbation of cycle-related symptoms
2 Missing periods with or without oestrogen deficiency symptoms
3 Anovulatory bleeding that may be heavy, prolonged and without warning
4 Bleed-free intervals increase
5 Menopause is the last cyclical bleed – typically age 51-52 but 1% are <40 (this is termed premature ovarian insufficiency [POI])

Chaotic, intermenstrual or postcoital bleeding should be investigated.

Symptoms consistent with oestrogen deficiency
- Vasomotor
  - Daytime flushes
  - Night sweats
  - Palpitations
- Sleep disturbance
- Mood change
- Memory, concentration and decision making change
- Tiredness and fatigue
- Loss of coping ability
- Joint pains
- Skin and hair change
- Urogenital atrophy affecting
  - Vagina
  - External genitalia
  - Bladder trigone and urethra
- Sexual function

These symptoms may or may not be recognised by the patient as menopause-related

Impact
What difference does this make to her life, work and relationships?
This may be devastating to some, particularly young women.

Evaluation

Evaluation
Age
- 45-55 is normal
  - Diagnosis is clinical – no tests needed
- 40-44 is early
  - Diagnosis is clinical – consider FSH to support if equivocal
- <40 is premature ovarian insufficiency (PO)
  - Diagnosis is clinical
  - If there is no bleeding, check FSH twice at 4-6 week intervals. This provides support for management – levels are raised if at the point of testing, ovarian response is deficient – with two raised results (>30IU/ml) ovarian response is consistently deficient, but this does not tell you for how long this has been the case or if there may be response in the future

If bleeding is still cyclical, FSH estimation is not indicated
Consider:
- Ongoing health issues
- Medication
- Previous medical history
- Family history
- Lifestyle

Risk assess in the fields of
- Gynaecology
  - Refer if red flags (e.g. intermenstrual, postcoital or postmenopausal bleeding)
- Breast
  - Seek expert advice if high risk
- Bone
  - Consider DXA and FRAX
- Cardiovascular
  - Seek advice if high risk
- Metabolism and endocrine
  - Seek advice if unsure
- Mental health
  - Consider previous intolerance to endogenous and exogenous hormones

Examine
- Blood pressure
- BMI
- Others only if indicated

Explain what is happening and its implications

Management

Management
Lifestyle advice
For symptoms and future health:
- Optimise weight (BMI 19-25)
- Consider exercise
  - Aim for 150 minutes of moderate exercise a week – ideally five sessions of 30 minutes
  - Consider walking to work, walking the dog more briskly etc. as weight-bearing exercise will also help bones
- Consider caffeine intake and reduce if necessary
- Consider calcium intake
  - 1000mg/day recommended
  - Incorporate a daily pint of milk into the diet
- Consider vitamin D exposure/intake
- Consider alcohol intake and reduce if necessary
  - <14 units a week

Discuss with the patient what she wants

Herbals
- Isoflavones (plant oestrogens)
  - Limited evidence of efficacy and less of toxicity
  - If purchased, recommend a standardised brand with THR logo
- Black cohosh
  - Evidence of some benefit in short term
  - Concern regarding liver effects still unclear

Non-hormonal prescribed options
- Clonidine 50mg twice daily – licensed
  - Not recommended by NICE – little benefit above placebo
  - Side-effect profile includes sleep disturbance
- Venlafaxine 37.5mg once daily and rising to twice daily but no more – unlicensed
  - Not recommended as first line by NICE but some benefit for flushing, sleep and mood
  - Adverse effect on blood pressure and sexual function
  - Consider in women for whom oestrogen is contraindicated
- SSRIs not recommended by NICE unless formally diagnosed with depression. Not indicated for menopause-related mood change
- Gabapentin – unlicensed though some evidence that 300-900mg/day will reduce flushing
  - Not recommended first-line
  - Too sedative for most women

Hormones
Vaginal low potency products
- All can be used unopposed at standard dosage – choose a product the patient will use
  - Estriol creams (0.1% and 0.01%)
  - Estradiol 10mcg vaginal tablet
  - Estradiol 7.5mcg/day vaginal ring
- Warn patients that these have no significant systemic activity, otherwise package information leaflet may cause alarm
- Avoid in hormone-dependent cancers unless patient-specific advice from expert otherwise available
- Use is recommended by NICE for as long as problem persists

Systemic
- Oestrogens
  - Oral
- Estradiol (E2)
- Conjugated equine oestrogens (CEE)
  - Non-oral
- Patches (E2)
- Gel (E2)

Tibolone – oestrogenic, progestogenic and androgenic properties
Testosterone – not licensed for women but may be indicated for a minority after specialist assessment

Considerations
Endometrial protection
- Needed if endometrium is present (including after ablation or if residual endometriosis)
- Use tibolone alone but use oestrogen with
  - Intrauterine progestogen at any stage
  or
  - Cyclical progestogen regimen if last menstrual period was <1 year ago, this should result in a predictable bleed acceptable to the patient. If intolerance occurs, you can identify the component responsible.
  - Continuous progestogen regimen if last menstrual period was >1 year ago as unscheduled bleeding then less likely.
  - Change to continuous combined at age 54 or within five years as this offers best protection Or
  - If experienced consider CEE/BZA (conjugated equine oestrogens 0.45mg with bazedoxifene. This is a selective oestrogen receptor modulator which opposes endometrial stimulation at the dose used)

Progestogen intolerance
- Discuss previous experience and contraception effects
- If intolerance suggested, consider
  - A ready-made combination using dydrogesterone (a progestogen derivative)
  - A bespoke regimen with micronised progesterone 100mg at night continuously or 200mg from day 15-26 (for a cyclical regimen)
  - this is an oral capsule but can be used vaginally off-license
  - Intrauterine progestogen (levonorgestrel intrauterine system – only Mirena is licensed)

Cardiovascular risks
- Any HRT started <10 years after last menstrual period reduces coronary artery disease
- If CVD risks are present but managed and oestrogen replacement desired, use a non-oral formulation to avoid increase in stroke and VTE risk
- HRT is not contraindicated in migraine but initiate with low dose transdermal and increase slowly to reduce the chance that a sudden increase will act as a trigger

Breast risks
- Consider individual risk profile and then any additional effect of HRT as this may not add further risk

Bone health
- Oestrogen has a dose-dependent effect on bone and standard HRT dosage has fracture prevention data at all sites and in unselected women. In POI, use to mean menopausal age protection would be recommended even if asymptomatic

Other medication
- Thyroxine – interaction via binding globulins – if dose is moderate or high, consider non-oral oestrogen
- Enzyme inducers - consider non-oral oestrogen

Oestrogen dose
- The oestrogen dose required is individual and is affected by many factors including absorption, protein binding, metabolic degradation and end organ sensitivity
- Estradiol 1.5-2mg oral/1.5mg transdermal gel/50mcg per day patch

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