Menopause Management

Dr Sonia Davison
Jean Hailes for Women's Health

Menopause

- Time of last menstrual period - average age 51
- Premature Menopause: occurs before age 40
- Perimenopause (menopause transition):
  - changes in pattern of menstruation
  - other symptoms often present
  - erratic hormone levels
  - can last 2-7 years
- Post menopause: no period for 12 months

Menopause symptoms

80% of women

- Vasomotor symptoms
  - Hot flushes
  - Night sweats
- Sleep disturbances
- Urogenital symptoms
  - Vaginal dryness
- Other symptoms
  - Formication
  - Joint pains
  - Difficulty concentrating
  - Irritability
  - Fatigue
  - Anxiety
  - Palpitations
  - Low mood

20% of women:

- NO symptoms
- SEVERE symptoms
- symptoms for > 5 years

Other causes of symptoms

- Exclude other causes if history is atypical
- Fatigue - iron studies, FBE, RBG
- Joint aching - rheumatological causes
- Mood disorders - depression, anxiety
- Thyroid disease

Ideal opportunity for a general check up (BP, cholesterol, cervical screening etc)

Management options

- Education
- Lifestyle
  - diet
  - exercise
  - smoking
  - alcohol
  - stress management
- MHT
- Complementary therapies
- Non-hormonal therapies

Menopausal hormone therapy (= Hormone replacement therapy)

- Well established for menopause symptom relief
- Not **currently** recommended for the **prevention** of disease except in premature menopause
- Weigh up the benefits and risks for each individual. These differ for women around the time of menopause compared to older women
- International expert society guidelines for menopause management advise that for the majority of healthy women around the time of menopause, the benefits outweigh the small risks

Types of MHT

- Oestrogen alone (E)
- Oestrogen plus Progestogen (E&P)
  - For endometrial protection
  - Cyclical regimen in peri - & early post menopause
  - Continuous in women more than 1 year post menopause
- Low dose OC pill in women <50 years old without significant CVRF, non smokers, no VTE
- Tibolone

Different routes MHT

- Oral (tablet and capsule)
- Transdermal - patch, gel
- Vaginal (oestrogen)
- Intrauterine (Mirena – levonorgestrel)

Different dosages of oestrogens

- Oral: 0.3 → 0.625mg CEE
  0.5 → 2mg 17β oestradiol
- Transdermal oestradiol 25 → 100μg
- 0.5 – 1mg oestradiol gel

- Prefer lowest effective dose, for shortest duration

- Australasian Menopause Society information sheet - "AMS Guide to equivalent MHT/HRT doses": https://www.menopause.org.au/hp/information-sheets/426-ams-guide-to-equivalent-mht-hrt-doses
- National Prescriber Service: http://www.nps.org.au/__data/assets/pdf_file/0008/76148/NPS_EVC_Menopause_Inser.pdf

On PBS

Oestrogens
- Progynova, Zumenon (tablets)
- Climara, Estradot, Estraderm MX (patches)
- Sandrena (gel)

Progestogens
- Provera, Primolut N (tablets)

Combination E+P
- Estalis continuous / sequi (patches)
- Femoston conti, 1mg/10mg, 2mg/10mg (tablets)

Not on PBS

Oestrogens
- Premarin, Estrofem (tablets)
- Estrogel (gel)

Progestogens
- Prometrium (capsules)

Other (tablets)
- Livial (Tibolone)
- Duavive (conjugated oestrogen and SERM)

Combination E+P (tablets)
- Trisequens (cyclical)
- Kliogest, Kliovance (continuous)
- Angeliq (continuous)

Jean Hailes FOR WOMEN'S HEALTH

Benefits of MHT

- Relief of menopausal symptoms
  ↓ hot flush frequency by 77%; ↓ severity by 87%
  MacLennan A, Lester S, Moore V (Cochrane Review Issue 3, 2004)
- Reduction of osteoporotic fracture risk:
  - MHT decreases the incidence of all osteoporosis related fractures, including vertebral and hip
  - first line therapy for post menopausal women <60 years old who are at high risk of fracture
  - in women with premature menopause
- Reduction of colorectal cancer risk
- Possible cardio-protection in women who start MHT < 60 years of age

Jean Hailes FOR WOMEN'S HEALTH

MHT and urogenital atrophy

- Topical vaginal oestrogen most efficacious treatment
- Added progestin is not required
- Systemic MHT may provide relief
- (Vaginal candidiasis is rare in post menopausal women)

Jean Hailes FOR WOMEN'S HEALTH

MHT and cardiovascular disease

- MHT started within 7 – 10 years of menopause may reduce the risk of cardiovascular disease

  ("window of opportunity")
- HOWEVER increased risk of CVD in women who start MHT after 60 years of age or with pre-existing CVD, mainly in women > 70 years using oral conjugated oestrogens and MPA (WHI study)

Adverse effects of MHT

- Breast cancer
- Cerebrovascular disease
- Venous thromboembolism

MHT and breast cancer

Combined MHT:
- Small increased risk after approximately 5 years use (randomised, placebo-controlled study data)
- Absolute risk increase varies from 0-12 additional cases per 1000 women per 5 years
- Different progestogens have different effects on breast cancer risk, with dydrogesterone and micronised progesterone having a lesser risk compared with medroxy-progesterone acetate

Oestrogen alone:
- Probably no effect on incidence of breast cancer (randomised, placebo-controlled study data)
- Annual breast examination and biennial mammogram

MHT and cardiovascular disease

- MHT should not be initiated for the secondary prevention of CVD
- There may be a place for using transdermal MHT in women at risk of CVD needing symptom relief
- Currently primary prevention is not an indication for MHT, but is open to further investigation

  ("window of opportunity")

MHT and cerebrovascular disease

- No impact in women <60 years old
- May cause small increase in women >60 years

MHT and venous thromboembolic disease

- Absolute risk increases with age
  - 1/10,000 women-years aged 50
  - 1/1000 women-years aged 60
  - 1/100 aged 80
- Increased risk with additional factors:
  - immobility, lower limb trauma, surgery hereditary thrombophilias, smoking, obesity
- 4 fold risk in first year,
  2 fold ongoing risk with combined MHT
- Low risk with oestrogen alone
- No increased risk with transdermal MHT
- No increased risk with tibolone

Endometrial cancer

- No increase in women on combined MHT
- Well documented increase with systemic oestrogen-alone in women with an intact uterus

Review treatment

- Initial – 3 months
  - Assess side effects and address concerns
- Annual review
  - Assess need, risks and benefits
  - Consider screening tests
  - Titrate dose

Side effects MHT

- Bleeding pattern
- Breast tenderness
- Progestogenic side effects - acne, mood changes
- Poor symptom control

(Weight increase - due to age)

Tibolone (Livial®)

- Synthetic steroid metabolized in a tissue-selective fashion:
- Oestrogenic effects:
  - bone, vagina and symptoms, but not on breast
- Progestogenic effect on endometrium
- Androgenic effects
  - Improves hormonal aspect of libido
- Low dose MHT
- Reduces risk of osteoporotic fractures
- Minimal breast tenderness
- No increase in VTE
- Increased stroke in women > 60 years
- Not appropriate in peri-menopausal women

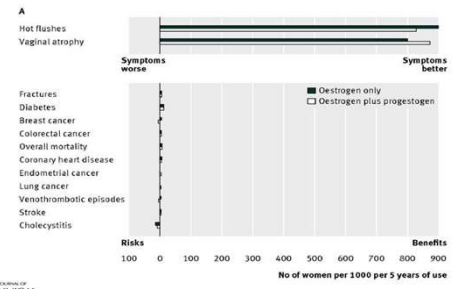
TSEC = Duavive (®)

- Combination of conjugated oestrogens and baxedoxifene (= selective oestrogen receptor modulator)
- No need for additional progestogen
- Low-medium dose MHT tablet
- May be useful if other progestogens not tolerated

Summary - MHT

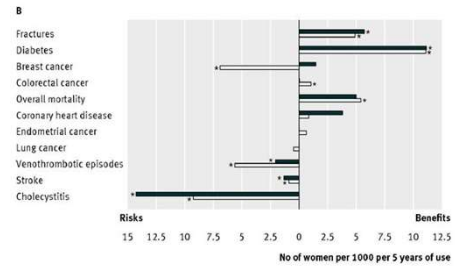
- Use lowest effective dose
- Assess benefits and risks annually
- Decrease dose or cease every few years to assess ongoing need for treatment
- Some women have ongoing symptoms and warrant ongoing MHT use

Risks and benefits of MHT between 50-59 yrs or <10 yrs after menopause



Santen R J et al. JCEM 2010;95:s1-s66

Risks and benefits of MHT between 50-59 yrs or <10 yrs after menopause



Santen R J et al. JCEM 2010;95:s1-s66

Other treatments (If women cannot take MHT)

- SNRI - venlafaxine (37.5-75 mg), desvenlafaxine
- SSRIs - paroxetine, fluoxetine, sertraline *(n.b. avoid use of these in women with breast cancer taking **tamoxifen** as they are inhibitors of CYP2D6 which is necessary for tamoxifen to become active; other options: citalopram, escitalopram)*
- Gabapentin (100mg/d for 3 days, increasing to b.d., then t.d.s. Max 900mg/d)
- Clonidine (25mcg b.d. for 2 weeks, increasing to max. 75mcg b.d.)

Testosterone therapy

- No clear definition of female androgen deficiency
- Difficulty with assays in women – request:
  sensitive (total) testosterone
  SHBG
  calculated free testosterone
- Not approved by TGA for use in women
- Consider Andro-feme cream
- Need to monitor rigorously

Herbal medicines

- Limited number of RCTs published, mainly small numbers and short duration
- Women may be self-prescribing, or advised inappropriately by practitioners or advertising
- Seek advice from trained Naturopath with women's health expertise

Black Cohosh (Remifemin®)

- Some evidence of efficacy for menopause symptoms
- Risk of liver damage in rare instances
- Commonly combined with St. John's Wort for anxiety or depression (drug interactions
  e.g. SSRIs, antiepileptics, oestrogens)

Phytoestrogens

- Plant foods with oestrogen-like activity

  (soy, linseed, grains, seeds, legumes, sprouts)
- Possible small effect on hot flushes
- Part of a healthy diet
- Especially beneficial for cardiovascular health

Bioidenticals

- Combinations of hormones in a troche (lozenge) or gel
  - eg. oestrogen, progesterone, testosterone, DHEA
- Manufactured in compounding pharmacies
- Not approved for use in Australia by TGA; medico-legal indemnity questionable
- Minimal data on efficacy and safety
- Some concerns regarding endometrial carcinoma
- Expensive, marketing is misleading

- **If women are seeking 'natural' hormone therapy 'body-identical' MHT can be prescribed (= combination of any oestradiol product and micronised progesterone <Prometrium®>; these hormones are identical to ovarian oestradiol and progesterone but have undergone rigorous safety testing and are approved by the TGA)**

Conclusion

Give well informed and up-to-date advice

- Websites:

  www.jeanhailes.org.au (Jean Hailes)

  www.menopause.org.au (AMS)

  www.menopause.org (NAMS)

  www.imsociety.ord (IMS)

Thank you

Jean Hailes FOR WOMEN'S HEALTH

Healthcare Education Research

www.jeanhailes.org.au