Menopause Management Update 2016

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Disclosure statement

Expert panel & consultant in last 5 years
• Bayer HealthCare
• Pfizer
• Flordis

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Take home messages

• Menopause is a clinical diagnosis with the menopause consultation ideal for preventative health interventions
• Evidence-based options are available for women experiencing vasomotor symptoms
• Provide information on the risks and benefits of treatment options including MHT & non-hormonal alternatives
• Initiate MHT before 60 or within 10 years of menopause (use the lowest dose for symptom control with annual monitoring)
• Women with urogenital symptoms can benefit from topical estrogen
• Women with premature menopause should be prescribed hormone therapy until the age of 51 usually high dose.

Today

• Defining menopause
• Diagnosing menopause & menopausal symptoms
• The menopausal consultation
• Understanding menopausal hormone therapy (MHT) in 2016
• Non-hormonal options for vasomotor symptom relief
• A critical review of complementary and bioidentical therapies
• Management of urogenital symptoms of menopause
• Summing up!

Defining menopause

Menopause
• The final menstrual period (median age 50-52 years)

Perimenopause
• The transition from onset of menstrual irregularity or symptoms until 12 months after the FMP (up to 10 years)

Post-menopause
• 12 months after the final menstrual period

Early menopause
• Last period between 40 and 45 years

Premature menopause (premature ovarian insufficiency POI)
• Last period before 40 years
• May be spontaneous or induced by surgery or cancer treatment (symptoms generally more severe)

Diagnosing menopause: the history makes the diagnosis

Don’t
• Check FSH, LH, estradiol or testosterone in a woman at the normal age of menopause
• Indications for intervention are clinical; blood test results will not influence management decisions

Do
• Take a good history; consider a symptom score card
• Consider other causes for symptoms
• Record personal and family history of medical conditions that may influence management
• Take a menstrual history
• Remember that menopause is an excellent opportunity to reinforce key preventative health messages
The symptoms of menopause

Perimenopause can include symptoms of both high or low estrogen levels

Symptoms related to estrogen deficiency include:

- **Central**: vasomotor symptoms, insomnia, mood changes
- **Joint**: aches & muscle pains
- **Urogenital**: vaginal dryness, urinary symptoms
- **Skin**: dryness, thinning, formation, loss of elasticity
- **Hair**: facial hair growth, scalp and pubic hair loss
- **Libido**

**Long term consequences**: metabolic, CV, brain, bone

- 20% of women have few or no symptoms
- 60% have 4-8 years of symptoms which can decrease quality of life
- 20% may have severe symptoms that continue into their 60s and 70s

Meeting Carole

Perimenopausal symptoms:

- 52 years
- Bothered by hot flushes for past 6 months with sleep disturbance
- LMP 6 months ago (irregular menses previous 12m)
- Married for 3 years
- Generally good health; well controlled hypertension
- Worries about weight gain

How would you manage Carole’s concerns?

The mid life consultation: What to consider

- Pre-menopausal
- Peri- and early menopausal
- Post-menopausal: Less than 65 yrs old within 10 years of LMP

- Health concerns including family history, general health and disease management
- Lifestyle issues such as smoking, alcohol, physical activity, diet and BMI
- Contraceptive requirements

- Management:
  - Menopausal symptoms
  - Vaginal symptoms
  - Sexual dysfunction
  - Osteoporosis prevention

- The menopausal consultation

- You may not be able to cover everything in one consultation
- 1st visit - history, information, initiating check-ups
- Concentrate initially on the woman’s top three concerns
- Always investigate abnormal bleeding
- Review need for contraception
- Give plan of management which will be reviewed at 2nd visit including results & therapy; – consider psychosocial issues and lifestyle measures (smoking, exercise, calcium, alcohol, weight)
- Provide written information (patient may feel quite desperate)

Carole is interested in hormone therapy:

Consider Contraindications to MHT

- Current, past or suspected breast cancer
- Known or suspected estrogen dependent malignancy
- Undiagnosed PV bleeding
- Untreated endometrial hyperplasia
- Current VTE (past history of VTE requires further investigation)
- Untreated hypertension (treated HT is not a contraindication)
- Active liver disease
- Porphyria cutanea tarda
- Known sensitivity to active substances or excipients

Menopausal Hormone Therapy: an overview

- Alleviate menopausal symptoms using the lowest possible estrogen dose
- MHT also provides: osteoporosis prevention, favourable for cardiovascular disease; colon cancer risk reduction
- Dose and duration - consistent with treatment goals
- ‘Estrogen only’ MHT - women after a hysterectomy
- Combined MHT should be used when the uterus is present (use cyclical therapy for women within 1 year of menopause then switch to continuous)
- Topical low dose estrogen for urogenital symptoms

Adapted from Updated IMS position statement 2013, Climacteric 2013; 16: 316-337
MHT: a 2016 approach to risks and benefits

- A decade of women missed out on MHT treatment due to confusing and conflicting information and media.
- The Women’s Health Initiative (WHI) trial was designed to investigate chronic disease in older women randomised to CEE + MPA vs placebo; trial stopped in 2002 due to safety concerns.
- Re-evaluated WHI data
  - MHT safe for healthy younger symptomatic women at the time of menopause with low risk of stroke and VTE.
  - Increased risk of breast cancer after 7 years of use (RR 1.28) for women in the treatment arm.
  - Multiple trials support the ‘safe window’ for prescribing:
    - <60 years or within 10 years of last menstrual period.
- Younger women more likely to be symptomatic, have lower risks for VTE and stroke, are more likely to derive cardiovascular benefit.

Women and MHT: Dose, delivery systems and regimens matter

Low dose therapy has:
- Less effect on thromboembolic risk
- Less effect on breast cancer risk

Transdermal therapy has:
- Less effect on thromboembolic risk
- Less effect on stroke risk

Estrogen alone has:
- Less effect on cardiovascular risk
- Less effect on VTE risk
- Less effect on breast cancer risk and colorectal cancer risk reduction

Not all progestins are created equal:
- Micronised progesterone & dydrogesterone has less effect on breast cancer risk (vs MPA and NETA)

Management options: intact uterus

- Transdermal estradiol preferred, combined patch:
  - one estradiol strength
  - two different progesterin doses
  - cyclical and continuous regimens
- Transdermal estradiol plus oral progesterone/dydrogesterone may be associated with less adverse effects on the breast and less progestogenic side effects.
- Transdermal or oral estradiol plus Mirena is a convenient regimen.
- Oral combined therapy popular and convenient.
- Tibolone has different characteristics to conventional MHT:
  - Only post-menopausal women
  - Especially low libido
  - Breast tenderness & high breast density

Management options: post hysterectomy

- Only estrogen is required
  - Exception: after surgery for endometriosis or endometrial cancer progestogens may sometimes be desirable (at least short term) to suppress residual endometrial cells.
  - Always use the lowest effective dose; titrate according to symptoms and side effects.
  - Oral estradiol alone has less VTE risk than oral E+P.
  - Transdermal delivery of estradiol reduces VTE risk.
  - Tibolone has less VTE risk than estradiol.

Carole decides to use a combined continuous patch but is worried about weight gain.

- 45 – 55 yrs women gain on average
  0.5 kg a year
- Linked to aging & environmental factors; not ‘caused’ by menopause.
- BUT abdominal fat deposition is associated with reduced estrogen.
- MHT does not cause weight gain.
- MHT can prevent abdominal fat deposition after menopause.
How long to continue treatment for menopause symptoms?

- MHT should be initiated before the age of 60
- No set minimum or maximum duration for using MHT
- Mean duration of hot flushes is 8 years;
  - 10% women experience more than 10 years of bothersome symptoms
- Recommend yearly review & every few years trial lower dose/consider stopping
- If symptoms return re-discuss risks and benefits according to history
  - ? investigate for secondary causes
- Premature ovarian insufficiency - continue high dose MHT until at least age 51 years

Meeting Kim:

Post menopausal with complex medical history

- Age 52 years
- hot flushes ‘day and night’
- LMP 2 years ago
- Past history of DVT and pulmonary embolus after breaking femur in skiing accident age 43
- Told “don’t ever take hormones”

Non-hormonal treatment options for vasomotor symptoms

Prescribed medications shown in RCTs to have evidence for efficacy and safety in the treatment

Note: ‘off label use’:

- SSRI/SNRI anti-depressants/anti-anxiety medications: effective in some women with added benefits on mood
  - See menopause.org.au for doses
- Caution in women on tamoxifen (paroxetine may reduce efficacy; venlafaxine and desvenlafaxine appear to be safe options)
- Gabapentin anti-epileptic: equivalent to estrogen in efficacy
- Pregabalin (neuropathic pain)
- Clonidine – mixed trial results, effect modest (side effects dose related)

Complementary medications

- Black cohosh: inconsistent effect (rare cases of liver failure)
- Red clover: no effect
- Soy-based: limited evidence
- Vitamin E: no effect
- Evening Primrose Oil: no effect

‘...data are insufficient to support the effectiveness of any complementary and alternative therapy in this review for the management of menopausal symptoms...’

Don’t prescribe “bio-identical” compounded hormones

- Evidence lacking for superiority claims
- Evidence lacking for quality, safety, efficacy
- Risks of compounded hormones not well documented because formulations are not tested in clinical trials before being dispensed; no formal mechanism for reporting adverse events
- AMS does not support their use
- FDA and North American Menopause Society (NAMS) have major warnings about their use
- Bio-identical progestins may be ineffective at reducing endometrial thickening and protecting the endometrium

Meeting Sara:

- 56 years
- Post-menopausal for 4 years
- No longer has hot flushes but experiencing dyspareunia with lack of lubrication on intercourse
- Has previously felt too embarrassed to seek help....
Genitourinary Syndrome of the Menopause (GSM) previously vulvovaginal atrophy

- Affects approx. 50% of women (few receive therapy)
- Vaginal dryness, dyspareunia and urinary symptoms; related to low estrogen, changes in vaginal flora & pH
- Topical preparations should be 1st choice
  - Ovexin cream and ovules (1mg estriol per G); vagifem tablets (10ug estradiol); daily for 2 weeks then 2 x weekly; progestins not required with this regimen
  - Use of vaginal estrogen for women with a hormone-dependent cancer is controversial (contraindicated in women taking aromatase inhibitors)
  - Non-hormonal vaginal moisturisers are available
  - Vaginal laser therapy - insufficient long term data available

Take home messages

- Menopause is a clinical diagnosis, think preventative health interventions
- Evidence-based options for vasomotor symptoms
- Premature menopause – High dose MHT until the age of 51
- MHT controls symptoms, bone and cardiovascular health benefits
  - Initiate MHT before 60 or within 10 years of menopause
  - Lowest dose to control symptoms and monitor annually
  - Transdermal E appears to offer the 'best' risk to benefit outcome (individual choice)
- Urinary symptoms - topical estrogen
- Prescribed non-hormonal alternatives can provide symptom-relief
- Don’t prescribe ‘bio-identical’ hormones
- Provide information on the risks and benefits of treatment options
- Support for women and practitioners is available at menopause.org.au
  jeanhailes.org.au

Resources

jeanhailes.org.au
  - Patient information & fact sheets
  - GP menopause management tool (pictured)
  - Green climacteric (symptom) scale
  - Health professional webinar library

menopause.org.au (Australasian Menopause Society)
  - A Practitioner’s Toolkit for the Management of the Menopause
  - Guide to HRT equivalent doses
  - AMS symptom score sheet
  - Patient information sheets