Menopause update

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donpowys meeting 13 oct 2016
Take home messages

• HRT is the most effective treatment for VMS
• Benefits outweigh risks if treatment started <60 or < 10yrs from final period
• There is no arbitrary upper age or time limit for taking it
• E2 only: no ↑ risk of Ca breast
Consensus that:

• HRT may improve joint & muscle pain, mood swings, disturbed sleep
• HRT is effective for genitourinary menopause symptoms
Guidelines differ...

- Try HRT for mood changes in woman > 45 (NICE)
- Use HRT for 1st line in fracture prevention (IMS, Revised Global Consensus)
- E & P appear to be cardioprotective (IMS)
- HRT may ↓ CHD and all cause mortality in <60s or <10 yrs after FMP (Revised global consensus)
- No justification for HRT to prevent CHD, breast cancer or dementia (NICE, Endocrine Society)
Robert Langer, principle investigator
for WHI: 2016

• ‘The paper that turned the world upside down’
• ‘The WHI has done a huge amount of unnecessary harm’
• Written without involving clinical investigators who tried to prevent publication till revised
• No adjustment for covariates
Menopause symptoms

- Pathognomic: flushes, sweats, vaginal dryness
- 70-80% women in western culture
- 45% find them distressing
- 18% consulted GP in 1996 → 10% in 2010
- Median = 7 years, 15% 20 yrs+

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Other symptoms

- Loss of concentration
- Forgetfulness
- Loss of libido
- Loss of confidence
- Indecisiveness
- Emotional lability
- Panic attacks
- Dry skin/ hair
- Joints ache
- Stiffness
- Palpitations
- No energy
Difficult time of life

- Ageing/dependent parents
- Death of parent/relative/friend
- Loss of partner - death/divorce
- Social isolation
- Empty nest/ redundancy
- Children problems
- Sudden evidence of ageing
- Loss of youth/fertility in youth-loving culture

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Self image
Oestrogen

- Excellent in reducing vasomotor + vaginal symptoms
- May help with other symptoms
- Side effects unusual: nausea, mastalgia, fluid retention
- Route/type traditionally unimportant, but transdermal fashionable as it does not ↑ VTE, CVA risk
- Equine oestrogens less fashionable
- Women vary in how well they absorb via different routes. Measuring levels is unreliable with oral Rx
Oestrogen: routes and doses

• Tablet daily
• Patch (3-7 days, can fall off, 1 in 7 get rash)
• Transdermal gel daily (dries in 2-3 mins)
• Implant (surgical procedure, tachyphylaxis)
• Ring (British women don’t like them)
• Standard bone conserving doses:
oestradiol valerate 2mg
(conjugated equine oestrogens 0.625mg)
17 beta-oestradiol 50ug patch
50 mg implant
• standard, double, half doses
Bio- what?

Bio-identical
- Estrone E1
- Estradiol E2
- Estriol E3
- Progesterone

Non bio-identical
- Ethinylestradiol
- Conjugated EE
- Mestranol (norinyl1)
- Progestagens: MPA, NE, drospirenone, LNG, gestodene, desogestrel
Proportion of different oestrogens in women and horses

From ‘Prevention & treatment of VTE during HRT: current perspectives’
H Rott, Int Gen Med 2014; 7:433
Complementary therapies NICE

• The efficacy and safety of unregulated compounded bioidentical hormones are unknown.

• Although there is some evidence that isoflavones or black cohosh may help VMS, their safety is unknown and purity and constituents of products may be unknown.

• St John’s wort may be a treatment option for menopausal mood symptoms but can interact with other medicines (eg, tamoxifen).
Progestogens

• Only needed if intact uterus (even if endometrium ablated). Reduces \( \uparrow \) risk ca endometrium in cyclical Rx, ‘abolishes’ it with CC Rx

• Different Ps have different effects on lipids: progesterone least effect

• Side effects: bleeding, PMS effects

• Reduce side-effects by changing type or route eg: IUS, transdermal, vaginal

• Routes: patch, tablet, vaginal cream, IUS (5 yr licence)
Tibolone (Livial)

- Synthetic, much less data, risks as for HRT
- Marketed as E+P+T type actions all in one
- Continuous combined action - suitable only for post menopausal women
- ‘bleed free’
- Anecdotally: less effective at reducing vasomotor symptoms than E
- No increased density of breast tissue on mammogram
Testosterone

- Produced from stroma of ovary and adrenals. Levels drop steadily > age 20, no sudden drop at menopause
- Associated with ↑ energy, drive, libido.
- May help with flushes
- Clearly indicated in castrated women with symptoms, but other women can benefit
- *** address relationship issues with libido 1st***
- Ensure fully oestrogenised first
- Common SE’s: spotty skin, body hair coarser
- Less long term safety data
- Routes: gel (~ ¼ dose mens’ preparation) Implant & patch discontinued (not commercial)
Starting HRT

• What for? Record top 3 symptoms
• Who?
• Examination? no
• Investigations? Only if <40
• Contraindications? – not absolute Ca breast or high risk VTE or high risk
• Information, websites
• Follow up

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<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>• Intolerable VMS</td>
<td>• Breast or endometrial cancer</td>
</tr>
<tr>
<td>• Vaginal symptoms</td>
<td>• Oestrogen provoked VTE</td>
</tr>
<tr>
<td>• Low mood</td>
<td></td>
</tr>
<tr>
<td>• Musculoskeletal</td>
<td></td>
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<tr>
<td>• Urogenital</td>
<td></td>
</tr>
<tr>
<td>• Sexual difficulties</td>
<td></td>
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<tr>
<td>• Premature menopause, Including iatrogenic</td>
<td></td>
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<td>(offer referral before Rx)</td>
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No contraindications

- Benign breast dis
- Cx, ovarian Ca
- Epilepsy
- Fibroids
- ↑ BP
- Otosclerosis
- Parkinsons
- RA

- Inflamm bowel dis
- Diabetes
- Gallstones
- Hyperlipidaemia
- Migraine
Surveillance

• Annual review recommended:
  To encourage compliance if POF
  To discuss risk/benefit if >60
  ? What is the value if 50-59 and happy on treatment

• No need for extra mammograms or other monitoring
Bleeding

• Normal in 1\textsuperscript{st} 3-6 months
• Change progestagen
• Change route
• Increase progestagen dose
• Reduce oestrogen dose
• Refer if persists > 6 months or after changes
Progesterone side effects

• PMS: irritability, bloating, constipation, acne
• Change progestagen (3rd generation better)
• Change route (transdermal or IUS better)
• Consider oestrogen only and endometrial monitoring (specialist care)
Libido

• Most important sexual organ is the BRAIN
• What part of libido?
• When was sex last good? What triggered the change?
  If oophorectomy → testosterone (gel)
  If dyspareunia examine and give local E2
• If good relationship can try testosterone, after ensuring adequate oestrogenisation
• (Livial?)
Background risk of Ca breast over 7.5 years in women aged 50-59 = 9/1,00000
RR of 1.2 = +2
RR of 2.7 = +24

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<table>
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<tr>
<th>Factor</th>
<th>Relative risk of Ca breast</th>
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<tbody>
<tr>
<td>&gt;2-3 u alcohol/day</td>
<td>1.5</td>
</tr>
<tr>
<td>obesity</td>
<td>1.6</td>
</tr>
<tr>
<td>&gt;30 yr @1st pregnancy</td>
<td>1.9</td>
</tr>
<tr>
<td>&gt; 5 yrs E+P</td>
<td>1.26</td>
</tr>
<tr>
<td>&gt; 5 yrs E only</td>
<td>1.0</td>
</tr>
<tr>
<td>Late menopause</td>
<td>Same as E+P</td>
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Stopping HRT

You want it how long?

• No arbitrary age limit or duration of treatment
• NB E2 only has no long term ↑risks
• Benefits outweigh risks for women in 50s
• After a few years > 50 have a whirl with ↓dose. Snip a patch in ½ or ¼ to taper off. If symptoms return ↑again.
• After 60 give data, assess lifestyle and allow woman to choose.
HRT ↑ QALYs
Patient centred care (NICE)

• The impact of severe menopausal symptoms on quality of life may be substantial and some women for whom HRT is contraindicated may choose to accept a degree of risk that might be considered by some to outweigh the benefits of MHT. A fully informed patient should be empowered and supported to make a decision that best balances benefits to that individual when weighed against potential risks.
Woman 53

- VMS since age 51.
- Cycle before starting HRT = 3-10/ 12-90
- Sterilized
- Started femoston 2/10 6 months ago
- VMS gone but having regular, heavy bleeds and IMB every cycle for several days, not settling
- What do you do?
Woman 49

• Cycle 5/28
• VMS and tiredness for 18 months: cant function in her job.
• Started Elleste Duet 1mg 3 months ago
• Flushes slightly better, but bloated, irritable, sore breasts. (Always had PMT.) Stopped taking it after 2 months.
• In new relationship, needs contraception, condoms so far.
Woman 43

• TAHBSO age 32, painful intercourse.
• Has been on oestrogen only HRT till last year when a colleague stopped it as she had been on it for 10 years.
• What do you do?
Woman, 54

- TATT, low mood, loss of libido last 2 years
- Occasional flushes soon after FMP 3 yr ago, not really problematic now
- ↑BP, ↑cholesterol, BMI 32
- Has had benign breast lump & endometrial ablation for heavy periods. Mother had Ca breast aged 56.
- Husband ‘very good really’
Thank you