CASE FIVE

Short case number: 3_29_5
Category: Endocrine and Reproductive Systems
Discipline: Obstetrics & Gynaecology
Setting: General Practice
Topic: Menopause

Case

Martha Heaney is a 53 year old woman who you know well. She is healthy, but is suffering from hot flushes and difficulty sleeping, and it is affecting her mood. She has not had a menstrual period for 9 months. She is happily married and has 3 adult children. Martha takes no regular medications and has no allergies. Her BMI is 27, she is a non-smoker and has 1 glass of wine every night.

Questions

1. Outline your history, examination, and any investigations you would want for Martha.
2. This consultation provides a good opportunity to discuss routine screening tests with Martha. Discuss the recommended screening programs that Martha should be aware of.
3. Briefly explain the menopausal hormone treatment (MHT) options using the following table

		Explanation
What	Oestrogen only (no uterus)	
	Oestrogen and progesterone (intact uterus)	
When	Continuous	
	Cyclical	
How	Oral	
	Topical/patch	
	IUD	

4. What are some non-hormonal menopausal treatment options?
5. Briefly discuss the effects that menopause has on the cardiovascular system and bone health.
6. The Women's Health Initiative (WHI) is a landmark study published in July 2002 in the Journal of the American Medical Association. Release of the study's results sparked alarm amongst the public and disharmony in the medical management of menopause. Briefly summarise the studies findings and identify one limitation of the study.

Suggested Reading

- **Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier**
- **Dewhurst's Textbook of Obstetrics & Gynaecology, Edmonds K [editor]. Blackwell Publishing. 2007. Chapter 47**

Additional reading

- Australian Doctor, Sex Hormones in Menopause A.Prof Bronwyn Stuckey 8th Sept 2006 http://search.ebscohost.com.ipacez.nd.edu.au/login.aspx?direct=true&db=anh&AN=22559825&site=ehost-live&scope=site

ANSWERS

Question 1: Outline your history, examination, and any investigations you would want for Sally.

History

- History of presenting complaint - hot flushes/difficulty sleeping/affecting mood - how long has this been happening for and how are they affecting her life?
- Menstrual/gynae history - any bleeding at all in the past 9 months? Is she sexually active, any post coital bleeding? CST history.
- Other symptoms of menopause - vaginal dryness, dyspareunia, urinary symptoms including UTIs, weight changes, joint aches, change in libido, anxiety
- Past medical history - hypertension, diabetes, cholesterol, migraines with aura, breast cancer, venous thromboembolism, stroke, osteoporosis, liver disease, mental health
- Surgical history - hysterectomy, any gynae surgeries?
- Medications, over the counter or natural therapies
- Family history - breast cancer, any other cancers, VTE or stroke, osteoporosis
- Social - home life, work, diet, smoking, alcohol, drug use

Examination

- Inspection, observations (BP, HR) and BMI
- Abdo/pelvis examination for masses and tenderness, CST if due
- Breast examination for lumps
- Thyroid

Investigations

- Diagnosis of menopause can be confirmed with FSH > 40IU/L on 2 occasions more than a month apart, however it is rarely needed, unless a woman presents with symptoms and is less than 40 years of age.

- Consider overall health assessment with FBC, EUCs, LFTs, fasting BSL, lipids, TSH, Vit D if in an at-risk population, as well as screening assessments if due, ie, CST, mammogram, FOBT

The history, examination and investigations should be targeted to identify if it is safe to start Sally on menopausal hormone therapy (MHT). You should keep the contraindications to MHT in your head when assessing her.

Question 2: This consultation provides a good opportunity to discuss routine screening tests with Sally. Discuss the recommended screening programs that Sally should be aware of.

1. Cervical screening test - recommended 5 yearly HPV DNA test for women up to the age of 74 years
2. Breast screening - recommended 2 yearly mammograms for women aged 50 to 74 years
3. Bowel cancer screening - recommended 2 yearly faecal occult blood test for people aged 50 to 74 years
4. Osteoporosis - a dual energy X-ray absorbtiometry (DEXA) scan (of the hip and spine) is the gold standard for calculating bone mineral density and diagnosing osteoporosis. Osteoporosis Australia advocate for anyone over the age of 50 years to have a DEXA scan if they have risk factors, or over 70 years regardless of risk factors. Risk factors include age >50 years for women plus any of:
    - family history of minimal trauma fractures
    - smoking
    - high alcohol intake (>2–4 standard drinks per day for men, less for women)
    - diet lacking in calcium
    - low body weight
    - recurrent falls
    - sedentary lifestyle over many years

Question 3: Briefly explain the menopausal hormone treatment (MHT) options using the following table

		Explanation
What	Oestrogen only (no uterus)	Oestrogen to alleviate menopausal symptoms, namely hot flushes, night sweats, vaginal dryness, sleep disturbance, mood changes.
	Oestrogen and progesterone (intact uterus)	Progesterone must be added to MHT regime if a woman has her uterus to avoid the effects of unopposed oestrogen, ie, it reduces the risk of endometrial cancer
When	Cyclical	Progesterone for 12 to 14 days of the cycle, usually given in the 2nd half of cycle. Recommended in the menopause transition, and when the period of amenorrhoea has been less than 12 months. It will give cyclical bleeding.

	Continuous	Recommended in women when amenorrhoeic for more than 12 months. If continuous progesterone is given before this, women tend to get bothersome breakthrough bleeding. Some spotting or breakthrough bleeding is common for the first 3-4 months of continuous progesterone, then amenorrhoea occurs in more than 90% of women.
How	Oral	Daily tablets. COCP can be used in women in the menopausal transition, and provide contraception. When contraception is no longer required, a lower dose MHT can be used, and both oestrogen and progesterone can be taking as pills
	Topical/patch	Combined or oestrogen-only patches usually applied twice per week, or an oestrogen gel applied daily. Local vaginal oestrogen cream can also be considered for urogenital symptoms
	IUD	Progesterone IUD is an option, and will provide continuous progesterone and contraception in those women who require it

Question 4: What are some non-hormonal menopausal treatment options?

For women with contraindications to hormonal therapy, treatment with the following non-hormonal therapies may provide some relief of vasomotor symptoms (VMS). They are not as effective as MHT however.

- SSRIs/SNRIs - Escitalopram, Paroxetine, Venlafaxine, Desvenlafaxine. These antidepressants have been shown to have modest improvements in the severity and frequency of VMS, and have the added benefit of improving mood in some women
- Clonidine - a centrally acting alpha agonist usually used as an anti-hypertensive. Only modest effects on VMS have been seen
- Gabapentin - an anti-epileptic drug, that has been shown to reduce VMS as well as having anxiolytic effects

Side effects of these medications include drowsiness, dizziness, and nausea, and Clonidine has the additional side effect of dry mouth. Use for the relief of VMS is often limited by adverse effects. It must also be remembered that they do not have the potential benefits for bone and cardiovascular health.

Hypnosis and cognitive behaviour therapy have both been shown to reduced VMS.
For severe VMS, a stellate ganglion block has been shown to be effective for up to 12 weeks.

Question 5: Briefly discuss the effects that menopause has on the cardiovascular system and bone health.

Cardiovascular health

Oestrogen deficiency is associated with increased visceral and central adiposity, and abnormal lipid profile. Activation of the renin-angiotensin pathway also occurs, with down regulation of a number of receptors, leading to abnormal endothelial function. This is associated with hypertension, type 2 diabetes, obesity, atherosclerosis, heart disease and stroke.

During the reproductive years women are largely protected from cardiovascular disease. With increasing age this advantage is lost, with heart disease the leading cause of death in women.

Bone health

During the menopause transition, there is rapid bone loss associated with declining oestrogen levels. It is thought that there is around 10-20% loss of bone density in women in the 5 years around the menopause. Ageing and a loss of oestrogen results in dominance of osteoclasts over osteoblasts, and net bone loss. In addition, low oestrogen levels are associated with greater responsiveness of bone to parathyroid hormone, resulting in activation of osteoclasts and more calcium being mobilised from bone.

Osteoporosis is marked by low bone mineral density and deterioration of bone tissue, making bones more fragile and at risk of fracture. Almost half of Australian women over the age of 60 years will be diagnosed with an osteoporotic fracture.

Question 6: Briefly summarise the studies findings and identify one limitation of the study.

- Women's Heath Initiative (WHI), JAMA, 2002
- Ran from 1993, study was stopped prematurely in 2002
- Consisted of 4 separate studies to look into major health issues causing morbidity and mortality in menopausal women
  - An RCT on low-fat diet, an RCT on calcium and vitamin supplementation, and two hormone therapy trials
  - It is the hormone trials that caused alarm amongst the medical field and women taking MHT

<u>Summary of findings</u>

In the combined MHT arm (oestrogen + progesterone), the WHI found an increased risk of heart disease, breast cancer, stroke and pulmonary embolism. There was a reduced risk for fracture and colorectal cancer, and no significant difference found in the risk for endometrial cancer or total mortality.

In the oestrogen-only arm, the WHI found an increased risk of stroke, a reduced risk of hip fracture, and no difference for heart disease, breast cancer, venous thromboembolism, colorectal cancer, or total mortality.

Some limitations

Difficult to generalise the findings

- The average age of the study population was 63 years, older than that of a typical MHT user, and only 3.5% were aged between 50-54 years
- Only 13% of women were within 5 years of menopause
- The majority of women in the trial were asymptomatic of menopausal symptoms. MHT would rarely be used in woman unless she were symptomatic.
- Only 30% of women in the trial were within the normal range for BMI

- Trial tested only 1 MHT regimen
- Quality of life was not an outcome
- There were high rates of discontinuation in the treatment arm (42%) and cross over to treatment from placebo (11%)

Problems with data dissemination

- Results of the trial were released at a press conference prior to being published in JAMA, and therefore were not reviewed by the medical field prior to consumer and media alert
- Media reporting of statistics was inaccurate
- Media reported relative risks not absolute risks, and although statistically significant relative risks were seen, absolute risks were very low, meaning that the incidence of an adverse event was rare
- Publication was said to be rushed, with investigators not having sufficient opportunity to review statistics

References

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4. RACGP and Osteoporosis Australia. Osteoporosis prevention, diagnosis, and management in postmenopausal women and men over 50 years of age (2nd Ed.). East Melbourne, Vic. RACGP, 2017.
5. RANZCOG. Managing menopausal symptoms (C-Gyn 9). Sept 2020.
6. Taylor H., Pal L., Seli E. Speroff's Clinical Gynaecologic Endocinology and Infertility, 9th ed. USA, 2019.
7. Women's Health Initiative. Hormone therapy trials. https://www.whi.org/about/SitePages/HT.aspx