Beyond Cancer: Living with an induced menopause

HRT after Gynaecological Cancer

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Declaration of Interests

Financial:
- Honoraria for lectures and consultancy from Besins, Theramex and Shionogi

Professional:
- Board Member of the British Menopause Society
- Board Member of the International Menopause Society
- Associate Editor of Climacteric
- Patron Daisy Network

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HRT AFTER GYNAECOLOGICAL CANCERS

- Background
- Generic Considerations for all cancers
- Endometrial cancer
- Ovarian Cancer
- Cervical Cancer
- Vulval and Vaginal Cancers
- Other non-gynaecological Cancers – Lung, Melanoma, Menigioma

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GYNAECOLOGICAL CANCERS BACKGROUND

- Prevalence 1.3 million worldwide, 21,500/annum in UK
- Cervix commonest then Endometrial worldwide
- Endometrial commonest in UK

- Treatment often includes hysterectomy + BSO
- Substantial number will be peri- or premenopausal
- Potential for sudden and early surgically induced menopause

- Symptoms maybe less discussed/recognized
- Ringing the Bell – and then falling off a cliff (Bell RJ Climacteric 2019 22:533-4)

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MENOPAUSE AFTER GYNAECOLOGICAL CANCERS

- Vasomotor symptoms (VMS) maybe more severe
- VMS can last 20 + years

- Vulvovaginal atrophy symptoms maybe particularly severe
- Radiotherapy or surgery can lead to vaginal scarring
- Impact of sexual dysfunction often underestimated
- 50-60 % amongst cancer survivors, varies with age and cancer. (Cust M BMJ 1989;299:1494-7, Schover L Climacteric 2019:6:533-7)

- Risk of osteoporosis maybe heightened
- Need for osteoporosis prevention strategy

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MENOPAUSE AFTER GYNAECOLOGICAL CANCERS

- Follow general management principles
- Behavioural and Lifestyle advice
- Consider CBT

- Specific management will depend on tumour type, staging and prognosis
- If not hormone dependent then no reason why HRT should not be considered

- Alternatives – limited evidence and safety concerns
- SSNRI's/Gabapentin/Neurokinins
- Specific vaginal and sexual health management
- Ongoing support essential

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HRT AFTER GYNAECOLOGICAL CANCERS

- HRT remains most effective treatment if not contraindicated
- HRT recommended for women with POI
- Reticence in use of HRT – patient and HCP

- Use lowest effective dose
- No need for progestogen if hysterectomized (exceptions)
- Consider Testosterone
- Overall safety should be emphasised
- Reassurance and follow up support maybe needed

- Vaginal oestrogen as well or on its own.
- Other vaginal preparations can be considered.

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Treatment Options for VVA

Vaginal

Lubricants and Moisturisers	Wide variety of products
Oestrogen preparations	Gold standard, NICE recommended
DHEA	12 month data
Laser	Preliminary data promising but invasive

Systemic

Oestrogens	Upto 25% women do not get relief
Ospemifene	Oral preparation that targets vagina. 12 week data but longer FU

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ENDOMETRIAL CANCER

- 4th commonest cancer in women (UK)
- 9,500 cases/annum
- 13% in crease over last 10 years – obesity and Tamoxifen
- Oestrogen dependent
- Nearly always requires Hysterectomy + BSO
- Predominantly post menopausal age group (peak 60-70)
- 20-25% occur in pre or peri-menopausal women.
- 5% < 40
- Lynch syndrome, obese, PCOS.
- Mostly early stage (I-II) with 5 year survival over 85%
- Quality of Life important

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ENDOMETRIAL CANCER

Management Options

- Tumour type and stage should be taken into account
- Risk of reactivation of residual disease
- Generally systemic HRT contraindicated
- Look at non-HRT options first
- Try non hormonal vaginal preparations first

Uterine Sarcomas
- Rare (< 5% uterine neoplasms)
- Maybe hormone dependent therefore receptor testing should be done (endometrial stromal sarcomas).
- If negative then HRT OK

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ENDOMETRIAL CANCER

- Limited evidence on HRT usage
- Mostly early stage disease
- Several observational studies, reassuring results

- RCT 3 year FU n = 1236 (Barakat RR et al J Clin Onc 2006;24:587-92)
- Mostly early stage disease
- Low recurrence in both groups

- Cochrane Review (Edey KA et al CD008830 2018)
  "Insufficient high quality evidence to inform women"
  No evidence of significant harm after early stage disease

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ENDOMETRIAL CANCER

National Comprehensive Cancer Network Panel
www.nccn.org 2019
- "Estrogen replacement is reasonable for those who are at low risk of recurrence (i.e. early stage disease) but treatment should be individualized and discussed in detail with the women."
- It also recommends waiting 6-12 months before initiating therapy.

North American Menopause Society (NAMS)
- Estrogen not recommended, use progestogen.

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ENDOMETRIAL CANCER
Recommendations:

- Always take into account stage of disease and time since diagnosis
- Avoid HRT if possible
- Vaginal oestrogen permissible but caution

- If QoL adversely effected then HRT can be used
- Use lowest possible dose
- Consider using progestogen - no specific data but potentially avoids reactivation of endometrial tissue.
- However balance against risk of combined HRT

- Patient should be fully aware of uncertainties and make the final decision

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OVARIAN CANCER

- Ovarian cancer is the leading cause of death from gynaecological cancer in the UK
- Sixth most common cancer in women, lifetime risk of about 2% in England and Wales.
- 7,400 new cases each year.
- 60% diagnosed in late stage
- The outcome generally poor, overall 5-year survival < 45%
- 90% 5 year survival in under 40's

- 95 % Epithelial cancer (3% germ cell, 2% sex-cord stromal)
- 5 types: High grade serous, Low grade serous, Endometrioid, Clear cell, Mucinous

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OVARIAN CANCER

- Generally HRT not contraindicated
- HRT has been "associated" with increased risk of ovarian cancer (Beral V et al Lancet 2015;385:1835-42)
- However overall risk very low (1 in 1000) and confined to serous and endometrioid types.

Several studies show no adverse effect of HRT on survival:

- 130 women, 4 year FU (Guidozzi F et al Cancer 1999;86:1013-8)
- No significant difference in survival or disease free interval
- N=150 any stage disease (Eeles R J Clin Oncol 2015;33:4138-44)
- Randomised HRT or not for 5 years
- 19 year FU, survival greater in HRT group.

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OVARIAN CANCER

- Cochrane Review (Saeaib N CD012559 2020)
- HRT slightly increases survival
- No conclusive evidence of HRT harm

- Endometrioid tumours are potentially oestrogen sensitive
- Consider adding progestogen

- Oestrogen not recommended in advanced disease of low grade serous tumours.
- Germ cell – young women. Prescribe HRT as normal
- Granulosa cell tumours – oestrogen sensitive. Avoid HRT
- Borderline – low malignant potential, no reason to avoid. Often younger women

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OVARIAN CANCER
Recommendations:

- Potential younger age group
- Overall HRT is OK and prescribe as normal
- Check tumour type
- Individualise treatment based on other factors
- Testosterone maybe useful
- Reassurance and support needed particularly for younger women

- Borderline and Germ Cell Tumours - HRT OK
- Endometrioid – caution
- Granulosa Cell – avoid HRT

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CERVICAL CANCER

- 14th commonest female cancer in UK
- 3,200 cases/year
- Decreased 25% over last 30 years
- Highest incidence in 30-34 age group

- 27,500 cases carcinoma in situ
- Increased 10 % over last 20 years
- Highest incidence in 25-29 age group

- Ovaries not necessarily removed
- Radiotherapy often used (40% cancers)
- 60% 5 year survival
- 90% 5 year survival in under 40s

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CERVICAL CANCER

- 85% Squamous Carcinoma
- Not hormone dependent
- Prescribe HRT as normal
- Use progestogen if uterus retained
- May need extra reassurance
- Additional support with sexual function e.g. counselling, dilators

- Adenocarcinoma (15%) potentially oestrogen sensitive
- Limited evidence of HRT use
- Treat as endometrial cancer but younger age may swing risks
- Abnormal smears are NOT a contra-indication to HRT

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VULVAL CANCER

- Uncommon
- Around 1300 cases per year
- Predominately in older age group (70+)
- 80% 5 year survival in under 50s
- Not oestrogen sensitive
- No increased risk with HRT (Persson I et al Cancer Causes Control 1999)
- Can prescribe HRT or vaginal oestrogens as appropriate
- Potential impact on sexual function both physically and psychologically.

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VAGINAL CANCER

- Rare
- 200 new cases/annum in UK
- Predominantly older age group
- 20% have major vaginal resection
- Potential impact on sexual function
- 80% 5 year survival in under 50's
- Diethylstilbestrol associated with clear cell cancer
- No increased risk with HRT (Persson I et al Cancer Causes Control 1999)
- Treat as cervical cancer

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NON-GYNAECOLOGICAL CANCERS and HRT

Lung Cancer
- Possible increase with E + P (Adami H Int J Cancer 1989, Statorte CJ J Clin Oncol 2010)
- Reduced risk of death with HRT RR 0.22 (Ettinger B Obstet Gynecol 1996)

Melanoma
- Possible oestrogen receptor status
- No increased incidence with HRT (Persson I Int J Cancer 1996)
- RR 1.24 with E only RR 0.91 E + P (Botteri E, Int J Cancer 2017)
- Data inconclusive (Hicks BM Human Reprod 2019)

Mengioma
- Often express ER and PR positive status
- No evidence tumour growth (Dresser L et al Sci Reports 2020)

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HRT AFTER GYNAECOLOGICAL CANCER

SUMMARY

- Gynaecological Cancer often effects peri or early postmenopausal women (POI)
- General menopausal advice and support
- Recommend multi-disciplinary approach
- HRT maybe appropriate
- Depends on age, impact, risk factors and tumour type
- Endometrial – caution
- Ovarian – generally HRT OK
- Cervical – HRT OK
- Vaginal symptoms and sexual dysfunction may require special attention
- Ongoing reassurance and support

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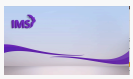
HRT AFTER GYNAECOLOGICAL CANCER

THANK YOU

ANY QUESTIONS?



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