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Review

Hormone replacement after gynaecological cancer

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ABSTRACT

Treatment of gynaecological cancer frequently results in the loss of ovarian function and menopausal symptoms. Symptoms of iatrogenic menopause are usually significantly more intense than those of natural menopause due to sudden onset of symptoms, younger age and its effects on common physical and psychological problems of cancer therapy like body image concerns and sexual dysfunction. The most effective treatment for menopausal symptoms is hormone replacement therapy (HRT). However, it is very controversial if HRT is safe in patients after a gynaecological malignancy. The main concerns are the potential stimulation of residual cancer and the induction of new hormone-dependent disease. However, the majority of the most common gynaecological malignancies like squamous cell carcinomas of the cervix, serous papillary epithelial ovarian carcinomas and squamous cell carcinomas of the vulva are not oestrogen dependent. Furthermore, current scientific evidence does not show HRT to adversely affect the outcome in patients after treatment for hormone sensitive cancers like early stage endometrioid adenocarcinomas of the endometrium. There are only a small number of gynaecological malignancies like low grade endometrial stromal sarcomas in which HRT is an absolute contraindication. Therefore, as maintaining quality of life and minimising the physical and psychological impact of treatment side effects is one of the most important factors in cancer care, it is imperative to give patients unbiased information about their individual cancer which in most cases will allow them to use HRT without any detrimental effect on their survival.

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1. Introduction

About 64,000 women will be diagnosed with a gynaecological cancer in the USA in 2009 [1]. Treatment usually involves radical surgery, chemotherapy and/or radiation resulting in loss of ovarian function and menopausal symptoms. Symptoms of iatrogenic menopause are usually significantly more intense than those of

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natural menopause due to sudden onset of symptoms, younger age and its effects on common physical and psychological problems of cancer therapy like body image concerns and sexual dysfunction.

The most effective treatment for menopausal symptoms is hormone replacement therapy (HRT). HRT consists of oestrogen which has to be combined with a progestogen in women with intact uterus to avoid the induction of proliferative endometrial changes like endometrial cancer. HRT is highly effective in improving menopausal symptoms like hot flushes, night sweats, dyspareunia, sexual function and insomnia and reduces the risk of fractures from osteoporosis [2–8].

Although HRT significantly improves quality of life of women with menopausal symptoms, it is an ongoing hotly debated subject whether HRT is safe in patients after treatment for gynaecological cancer [9].

The main concerns are the potential stimulation of hormone-dependent cancer and any residual endometrium. Furthermore, the controversial debate about potential long-term effects of HRT like the increased risk of breast cancer has complicated matters and consequently many physicians see HRT as being contraindicated [10,11].

As maintaining quality of life and minimising the physical and psychological impact of treatment side effects is one of the most important factors in cancer care the decision for or against HRT should be based on the available evidence. This review article therefore aims to provide an overview about the current knowledge regarding the safety of HRT after gynaecological cancer.

2. Endometrial cancer

Endometrial cancer (EC) is the most common gynaecological malignancy in developed countries [1]. It most commonly occurs in postmenopausal women, however, 20–25% of affected women are premenopausal and 5% are younger than 40 years [12].

The majority of endometrial cancers are diagnosed at an early stage (FIGO stage I–II) with a good overall prognosis and 5-year survival rate of over 85%. Consequently quality of life is an important issue for affected women. Treatment of endometrial cancer typically involves a hysterectomy and bilateral salpingo-oophorectomy. The adnexae are removed to exclude ovarian metastasis or a synchronous ovarian cancer, which occurs in 5% of cases. Radiotherapy is given as primary treatment in situations where the disease is locally advanced or the patient is unfit for surgery.

There are two types of EC: Type I accounts for about 90% of cases. It is an oestrogen-dependent cancer that tends to be endometrioid in cell type, oestrogen and progesterone receptor positive and generally presents with a lower grade. Type II EC occurs mainly in postmenopausal women and is not oestrogen-dependent. It tends to be of serous papillary or clear cell type; it is more aggressive with a higher histological grade, and lacks oestrogen and progesterone receptors. The risk factors for type I EC are well established and include unopposed oestrogen use and obesity. The hyperoestrogenic state in obese women can be caused by both chronic progesterone deficiency due to anovulation and enhanced peripheral conversion of androgens to oestrogens in peripheral adipose tissues [13].

As oestrogen plays such a prominent role in the carcinogenesis of the majority of endometrial cancers it seems to be contraindicated to replace this hormone after the disease has been treated. However, there is no evidence to substantiate the concern that HRT might adversely affect the outcome by stimulating the growth of occult tumour cells [14,15].

Various clinical studies have been performed on this topic and none has been able to show an increased risk of recurrence or mortality with oestrogen replacement after EC. Quite the contrary, an increased survival with oestrogen replacement therapy has been reported in some studies. Furthermore, no additional benefit of adding progestogens (combined HRT) has been found, although the studies are limited (Table 1) [16–23].

Forty-seven patients in a retrospective study by Creasman et al. used conjugated oestrogen by oral, vaginal and both oral and vaginal routes after stage 1 endometrial cancer. The ERT was initiated within a median interval of 15 months (0–81 months) after surgery. Lower recurrence rate of 2% vs. 15% and significant longer disease free and overall survival was seen in the ERT group in comparison to the controls [16].

Lee et al. compared 44 EC patients on HRT vs. 99 controls in their study. ERT was commenced within 12 months after treatment in 57% of the patients. No recurrence was observed in the ERT group, while 8% of patients in the control group relapsed. However, the ERT group consisted of younger patients with low risk features in comparison to the control group [19].

Chapman et al. examined 62 EC patients with stage 1 and 2 disease. The median time of initiation of postoperative oestrogen therapy was 8 months (0–108 months). Neither of the two groups displayed any significant difference in recurrence rate and overall survival although the data suggested an improved disease free survival in the ERT group. But the groups were not well matched as the patients in the control group more frequently had high-risk disease and were older than those taking ERT [20].

Suriano et al. published a comparative study on 75 FIGO stage 1–3 EC patients on ERT and a well-matched control group. The ERT was started within a 6 months period following surgery. A lower recurrence rate of 1% vs. 14% was observed for users and non-users, respectively. Patients on ERT also had significantly longer disease free interval [21].

Only two prospective studies have been conducted so far. The first by Ahyan et al. compared 50 patients and 52 well-matched controls with stage 1 and 2 EC. All patients received combined HRT within 4–8 weeks after surgery. No recurrence was noted in the HRT group, whereas one control recurred. The study, however, was non-randomised and the sample size was small [22].

The second study by Barakat et al. was a Gynaecologic Oncology Group study. It was a randomised double-blind prospective trial of HRT vs. placebo in women with early-stage EC. Between 1997 and 2003, about 1200 patients were included into the study. After publication of Women's Health Initiative (WHI) study in July 2002, enrolment decreased significantly and the study had to be closed prematurely as the accrual goal could not be reached. No statistically significant difference had been observed in the two groups at that stage [11,23].

3. Uterine sarcoma

Uterine sarcomas are a heterogenous group accounting for about 5% of uterine malignancies. The most common types are carcinosarcomas (malignant mixed mullerian tumours), leiomyosarcomas, and endometrial stromal sarcomas. Not much is known about their pathogenesis.

Leiomyosarcomas are accepted to be a non-hormone dependent disease allowing the preservation of the ovaries during the surgical treatment. In the few published case reports HRT did not have an adverse impact on patients after leiomyosarcoma treatment [24].

Carcinosarcomas, which more recently have been considered as a subtype of undifferentiated endometrial carcinomas, have been reported to have a potential link to hyperoestrogenism in rare, isolated cases [25,26]. However, no data is available regarding the safety of HRT after carcinosarcoma treatment.

Table 1
Studies on hormone replacement after endometrial cancer.

Author	Study design	HRT vs. controls (no. of patients)	Tumour stage	Type of HRT	Duration of HRT (months)	Duration of follow up (months)	Recurrence HRT vs. controls (no. of patients)	Study conclusions
Creasman et al. [16]	Case–control	47/174	Stage I	Conjugated oestrogen. Oral/vaginal/both	Mean 32 6–84	25–150	1 vs. 26	Endometrial cancer is not a contra-indication for HRT in patients with stage 1 disease
Byrant et al. [17]	Retrospective cohort	20	Stage I–II	Conjugated oestrogen with/without Depo Provera	12–132	42–168	No recurrence	No patient had a recurrence or died of intercurrent illnessess
Baker [18]	Retrospective cohort	31	NS	Oral/vaginal/transdermal oestrogen		16 years	No recurrence	The initial clinical data showed no increase in recurrence or mortality with ERT use
Lee et al. [19]	Case–control	44/99	Stage I	Oral oestrogen Oestrogen + progesterone	Median 64	24–84	0 vs. 8	Postoperative oestrogen replacement is safe in selected low risk patients
Chapman et al. [20]	Retrospective case–control	62/61	Surgical stage I–II	Oral/vaginal oestrogen with/without MPA 2.5 mg	Mean 49.1	Median 57.1	2 vs. 8	No evidence to suggest that oestrogen decreased the disease free interval or increased the risk for recurrence in early stage disease
Suriano et al. [21]	Retrospective cohort study with matched controls	75/75	Surgical stage I–III	Oral oestrogen with/without MPA 2.5 mg	Mean 83	Mean 83	2 vs. 11	ERT with or without progestogen does not appear to increase the rate of recurrence and death among EC survivors
Ayhan et al. [22]	Prospective case–control	50/52	Surgical stage I–II	Conjugated oestrogen 0.625 mg + 2.5 mg MPA	Mean 49.1 13–96	Mean 49.1	0 vs. 1	Immediate postoperative use of HRT did not increase the recurrence or death in EC survivors.
Barakat et al. [23]	Randomised double blind trial	618/618	Surgical stage I–II	Oral oestrogen	Planned duration 36	Median 35.7	14 vs. 12	Incomplete study. Cannot conclusively refute or support safety of exogenous oestrogen with regard to risk of endometrial cancer. Absolute recurrence rate 2.1% and incidence of new malignancy were low.

NS = not specified.

Low-grade endometrial stromal sarcomas (ESS) are steroid receptor positive and hormone sensitive malignancies. They account for only 0.2% of all gynaecological malignancies and occur mainly in pre- and peri-menopausal women. ESS have been reported to develop in the setting of hyperoestrogenism and have been linked to ovulation-stimulating drugs of assisted reproduction and HRT. After surgical treatment consisting of hysterectomy and bilateral salpingo-oophorectomy to ablate oestrogen production, patients are commonly receiving adjuvant progestogens and/or GnRH analogues with the aim to inhibit oestrogen-induced growth induction and recurrence [27].

Small case series studying women treated for ESS showed HRT to adversely affect the course of disease [28,29]. ERT is therefore contraindicated after low-grade endometrial stromal sarcomas [30].

4. Ovarian cancer

Ovarian cancer is the second most common gynaecological malignancy in developed countries. It has the highest mortality of all gynaecological cancers and the overall 5-year survival for all stages is only 45% [1].

Epithelial ovarian cancer (EOC) accounts for more than 90% of ovarian malignancies, while germ cell tumours (e.g. teratomas) and sex–cord stromal tumours (e.g. granulosa cell tumours) account for about 5% of malignant ovarian tumours each. The median age for diagnosis of EOC is 63 years (range 40–65) and also affects a significant number of premenopausal women [31,32].

EOC is classified into four main histological subtypes—serous, endometrioid, clear cell and mucinous carcinomas. Serous carcinomas account for 75% of EOC and are believed to originate from the surface epithelium of the ovary or the fimbrial end of the fallopian tube. Endometrioid and clear cell tumours are known to arise from ovarian inclusion cysts or foci of endometriosis. Ovarian endometrioid adenocarcinomas closely resemble endometrioid adenocarcinoma of the endometrium [33,34].

Borderline tumours of the ovary also known as tumours of low malignant potential (LMP) account for approximately 10% of epithelial ovarian neoplasms. They are commonly seen in premenopausal women with no known definite associated risk factors [35,36].

Steroid hormones especially androgens have been implicated in ovarian carcinogenesis with most tumours expressing high levels of androgen receptor concentration [37]. However, there is no convincing evidence that implicates oestrogen to act as an initiating or promoting factor for the development of EOC [10,32].

Two meta-analyses with conflicting results on the impact of HRT on EOC development have been published—the first suggesting no increase in relative risk of EOC in postmenopausal women taking HRT and a second showing a small, but significant, increase of risk after a prolonged use for more than 10 years [38,39].

Post-treatment, none of the published studies has shown an adverse effect of HRT on ovarian cancer patients (Table 2) [40–44].

Guidozzi et al. conducted a prospective randomised study in EOC patients to analyse the effect of ERT on survival. Conjugated oestrogens were given to 59 patients 6–8 weeks postoperatively. After a minimum follow up of 48 months no significant difference in survival was noted in the two groups and the study concluded that ERT could be given with a primary aim of improving quality of life in young EOC survivors without any adverse impact [41].

Mascarenhas et al. conducted a prospective cohort study and examined the effect of HRT before and after the diagnosis of both EOC and borderline tumours (BOT) on 5-year survival. The study included 649 EOC and 150 BOT of the ovary. It identified no clear differences in EOC survival among women who used any type of HRT before cancer diagnosis, and those who never used it. There was

Table 2
Studies on hormone replacement after ovarian cancer.

Author	Study design	HRT vs. controls (no. of patients)	Tumour stage	Type of HRT	Duration of HRT (months)	Duration of follow up (months)	Recurrence HRT vs. controls (no. of patients)	Study conclusions
Eeles et al. [40]	Retrospective case–control	78/295	Stage 1–2: 55% Stage 3–4: 45%	Oral oestrogen E+P E+T	Median 28	Median 42	–	HRT is unlikely to have a detrimental effect on prognosis of patients with ovarian cancer
Guidozzi and Daponte [41]	Randomised controlled trial	59/66	Stage 1–2: 27% Stage 3–4: 73%	Conjugated estrogen	28	Mean 42	32 vs.41	Postoperative oestrogen replacement did not have a negative influence on the disease free interval and overall survival of ovarian carcinoma survivors
Bebar et al. [42]	Retrospective cohort study	31/0	NS	Non-conjugated oestro-gen+progestogen	Mean 25	Mean 55	3	HRT does not seem to have noteworthy effect on progression of epithelial ovarian cancer
Ursic–Vrscaj et al. [43]	Retrospective case–control	24/48	Stage 1–2: 54% Stage 3: 46%	Non-conjugated oestrogen E+P E+T	Range 1–70 Mean 24	Mean 49	5 vs.15	HRT does not have pronounced effect on survival
Mascarenhas et al. [44]	Prospective cohort study	649 EOC 150 BOT	Stage 1–2: 60% Stage 3–4: 40%	Oestrogen E+P	Up to 24	60	–	Women using HRT after diagnosis had a better survival than women with no use

NS = not specified, E = oestrogen, P = progestogen, T = testosterone.

some indication of a better survival for users of HRT before diagnosis of a serous EOC, although without a clear pattern according to duration or recency of use. For the subgroup of endometrioid EOC similar results and no evidence of an association between HRT use before diagnosis was found. A better survival was found for women who used HRT after cancer diagnosis particularly among patients with serous types, but a better survival after endometrioid tumours was suggested too. For women with borderline ovarian tumours there were no associations between HRT-use pre- or post-diagnosis and survival [44].

Endometrioid EOC are oestrogen sensitive tumours and in theory residual disease after treatment could be stimulated by ERT. However, studies have failed to show an association between HRT use and the development of EC or the course of disease after treatment [44]. Conclusions can be extrapolated from studies on HRT use after treatment of endometrial cancer and ERT should be safe following treatment of early stage endometrioid EOC. However, it cannot be concluded that its' use is also safe in patients with stage 3 endometrioid adenocarcinomas who commonly have residual, potentially hormone responsive, disease after surgery.

BRCA 1 and 2 gene mutations are associated with increased risk of developing invasive EOC [35,36]. Data on HRT after prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers are sparse. However, none of the published studies shows an adverse effect of oestrogen replacement therapy following oophorectomy in those women [45,46].

Ovarian germ cell tumours (OGCT) commonly affect girls and young women between 10 and 30 years of age [47]. In most cases fertility preserving staging surgery is followed by platinum based combination chemotherapy (e.g. bleomycin + etoposide + cisplatin (BEP)) [48]. Gonadal dysfunction leading to transient or permanent ovarian failure can be a consequence of the chemotherapy [49]. No evidence is available to refute the use of HRT in this young patient group.

Granulosa cell tumours are the most common ovarian sex cord stromal tumours. They secrete steroid hormones and commonly present with symptoms of hyperoestrogenism. Fertility preserving surgery can be performed for stage 1 disease, whereas a total abdominal hysterectomy with removal of both adnexae is recommended for all other patients. Although no studies have been published regarding HRT after treatment for granulosa cell tumours of the ovary, the general belief is that it should not be used as it is endocrinologically active and hormone-dependent disease.

5. Cervical cancer

Cancer of the uterine cervix is the second most common malignancy and cause of significant morbidity and mortality in developing countries. The incidence of cervical cancer is age related—it rises to 1.7/100,000/year in women aged 20–24 years, with a second peak of 16.5/100,000/year in women aged 45–49 years [1]. Squamous cell carcinomas (SCC) account for approximately 80%, adenocarcinomas for 15%, and adeno-squamous lesions for about 5% of cervical cancers.

Fertility preserving surgery consisting of a conization or trachelectomy with or without lymph node dissection is an option for early stage disease (FIGO stage 1a1–stage 1b1) in women desiring to retain fertility, however the standard treatment consists of either radical surgery (radical hysterectomy including pelvic lymph node dissection) or alternatively primary chemo-radiotherapy.

The ovaries can be preserved in SCC of the cervix as the rate of metastasis is low (0.2% for stage 1b and 2% stage 2b disease). However, for adenocarcinomas the incidence of ovarian metastasis is much higher and about 4% for stage 1b disease and therefore many clinicians recommend an oophorectomy [50–52].

In patients with SCC or adenocarcinoma the preserved ovaries are commonly transposed out of the pelvis to avoid radiation damage if primary or adjuvant radiotherapy has to be given. Ovarian ablation can be expected to occur after radiation doses of 20 Gray (Gy) and is also dependent on ovarian reserve and age of the women. However, even with transposed ovaries, scatter radiation dose as low as 3 Gy induces menopausal symptoms in 20–28% of women and a dose up to 6 Gy causes premature gonadal dysfunction leading to ovarian failure in women over 40 years of age [53,54].

Patients receiving primary radiotherapy are treated with a combination of external beam radiation and vaginal brachytherapy. This is associated with significant radiation toxicity to the vagina like a partial vaginal stenosis (27% of cases) or even complete occlusion (11% of cases) [55]. Dyspareunia and major sexual dysfunctions are the consequences which warrant local oestrogen treatment.

SCC of the cervix is not considered to be oestrogen-responsive disease. Furthermore, HRT on its own does not seem to have a role in human papilloma virus (HPV) carriage or replication [57]. Some epidemiological data even suggests a protective effect of HRT [56].

For adenocarcinomas of the cervix, however, the findings are less conclusive. Epidemiological data have shown an increased risk association of adenocarcinoma of the cervix with prolonged use of oral contraceptive (OC) pills, more so in human papilloma virus (HPV) positive women. The mechanism of an increased cervical cancer risk in HPV-positive patients taking OC pills may be related to an oestrogen metabolite—16-alpha-hydroxyestrone, which acts as a cofactor together with oncogenic HPV to promote cell proliferation [58,59].

Furthermore, a case control study by Lacey et al. showed a significant correlation in between unopposed oestrogen therapy and adenocarcinoma of the cervix with an odds ratio (OR) of 2.7 [60].

No study to date, however, has shown an adverse effect of HRT after treatment of SCC or adenocarcinoma of the cervix (Table 3) [61].

Ploch et al. prospectively compared 80 HRT-users and 40 controls after surgery or radiotherapy for stage I or II cervical cancer over a period of 5 years. They found no difference in disease recurrence or overall survival in between the two groups. HRT optimally controlled most of the climacteric symptoms without any serious side effects and relieved bladder, rectal and vaginal post-radiological complications [61].

Patients whose cervical cancer is treated with primary radiotherapy retain their uterus. The uterus usually receives a total dose of 45–50 Gy during the treatment, which in the majority of cases causes complete and irreversible ablation of the endometrium. However, studies have shown that some residual endometrial tissue can potentially survive the treatment and respond to oestrogen therapy. It is therefore advisable to use combined HRT in patients with intact uterus treated with primary radiotherapy [62,63].

There is no evidence that local vaginal oestrogen application in form of creams or pessaries for radiation-induced side effects like vaginal stenosis could have an adverse effect on the course of a cervical cancer.

6. Vulval cancer

Vulvar cancer accounts for 5% of gynaecological cancers [1]. It is most frequently seen in postmenopausal women and the mean age of diagnosis is 65 years. However, an increasing incidence of HPV-related vulvar intraepithelial neoplasia among young women has been observed and may account for vulvar cancers at a younger age [64].

Table 3
Studies on hormone replacement after cervical cancer.

Author	Study design	HRT vs. controls (no. of patients)	Type of HRT	Duration of HRT (months)	Duration of follow up (months)	Recurrence HRT vs. control	Study conclusions
Ploch et al. [61]	Prospective case control	80/40	Trisequens/sequential dinestrol and chlormadinon	60	60	20% vs. 32%	No difference in OS or PFS. Patients can use HRT with aim of improving quality of life

OS = overall survival, PFS = progression free survival.

Squamous cell carcinomas (SCC) are the most common histological subtype and are seen in 90% of vulval cancer cases. It is a non-oestrogen dependent lesion. Other vulvar malignancies like adenocarcinomas originating from the Bartholin's gland or from Paget's disease are rare.

The need for local oestrogen treatment or systemic HRT may arise in women after vulvar cancer who had local radiotherapy or extended field radiotherapy to groin and pelvis in either the primary or adjuvant setting.

Epidemiological studies do not suggest an association of oestrogen use after menopause with VIN or invasive SCC of the vulva [10,65,66]. There is no evidence that HRT has a negative effect on the course of treated disease either. Systemic and topical oestrogens can therefore be used safely after a SCC of the vulva.

7. Vaginal cancer

Vaginal cancer accounts for approximately 0.3% of all gynaecological malignancies [1]. Squamous cell carcinomas (SCC) are the most common histological subtype followed by adenocarcinomas.

SCC of the vagina is usually a disease of postmenopausal women seen with increasing age and is very rarely seen women of younger age groups. SCC of vagina occurs mainly as a consequence of HPV related lower genital tract syndrome and very rarely due to post-radiation-induced carcinogenicity.

SCC of the vagina is generally accepted to be non-hormone dependent disease and there is no study to refute the use of local or systemic HRT after treatment.

Adenocarcinomas represent nearly all of the primary vaginal cancers in women less than 20 years of age [67]. Of those, clear-cell variants are seen in young women who have been exposed in utero to diethylstilbestrol (DES). The median age at diagnosis of DES-related clear cell adenocarcinoma of the vagina is 19 years, with a range of 7–33 years [68]. If ERT is safe in women treated for a DES-induced clear cell carcinomas of the vagina or in women exposed to DES in utero in general is unknown. Research on women exposed to DES in utero and HRT has been limited because most of them were born between late 1950s to 1970s and have yet to reach menopause. In absence of more definitive research prescribing HRT in these women should be made with caution.

8. Discussion

The safety of HRT after gynaecological cancer is a controversial topic. Unfortunately conclusive evidence cannot be drawn from the available data. However, based on the biological knowledge and published clinical information, SCCs of the uterine cervix, vulva and vagina as well as ovarian and endometrial serous carcinomas and most uterine sarcomas are not oestrogen-dependent and HRT can be given safely.

The question, however, is more complex regarding women with adenocarcinomas, in particular with endometrioid adenocarcinomas of the endometrium or the ovary. According to the results of the published, mostly retrospective case–control and cohort studies, HRT is not contraindicated after surgical treatment for early stage type I EC. However, the reason why HRT has not been shown to have an adverse effect might be the complete removal of the neoplasm and the surgical cure of the disease which is achieved in the majority of early stage ECs. Consequently, most women with early stage EC do not have any residual cells which could be stimulated by HRT.

The situation might be different in high risk or more advanced type I EC and more advanced (>stage Ia) endometrioid adenocarcinomas of the ovary. In those cases patients more commonly have hormone-responsive residual cells after treatment and con-

sequently HRT could have a detrimental effect on the course of the malignancy. One might speculate that the use of combined oestrogen–progestogen HRT with the aim to give progestogen to suppress oestrogen-stimulated growth would benefit patients under these circumstances but there is no evidence to support or reject this approach.

Therefore, for patients with more advanced endometrioid adenocarcinomas of the endometrium or ovary as well as with malignancies in which ERT is contraindicated, treatment of menopausal symptoms should be non-oestrogenic. In those cases progestogens and selective serotonin-reuptake inhibitors (SSRIs) are both known to alleviate vasomotor symptoms like hot flushes and the selective oestrogen receptor modulator raloxifene can protect against osteoporosis [69].

9. Conclusion

The available knowledge does not support the widespread concern about HRT for the majority of gynaecological malignancies. As maintaining quality of life and minimising the physical and psychological impact of treatment side effects is one of the most important factors in cancer care it should therefore be imperative to give patients unbiased information about their individual cancer which in most cases will allow them to use HRT without any adverse effect on their survival.

Conflict of interest

None declared.

Provenance

Commissioned and externally peer reviewed.

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