



Hormone replacement therapy (HRT) and hormonal contraception use in patients with meningioma: SBNS guidelines for neurosurgeons

- The following document has been developed for UK neurosurgeons to guide clinical consultations with patients with meningioma who are taking hormone replacement therapy
- Recommendations for clinical management should be made in consultation with patients

Risk factors for developing meningioma

1. *Ionizing radiation*: Irradiation for a variety of medical indications and also in atomic bomb survivors [1]. The risk of secondary tumours including meningiomas after radiosurgery is low with 6.8 cases per 100 000 patient-years [2].
2. *Type 2 neurofibromatosis (NF2)*: The most common genetic condition associated with meningioma. Patients are more likely to develop grade 2 and 3 or multiple meningiomas [3].

Links between HRT and hormonal contraception and meningioma

1. Studies have sought to link endogenous and exogenous hormone exposure to meningiomas because of higher incidence in women of reproductive age, tumour expression of hormone receptors (70-90% express progesterone), an association with breast cancer, and growth during pregnancy (and regression post-partum). Therefore some (not all) cranial meningioma are hormone sensitive. Routine progesterone and oestrogen receptor testing does not predict hormone-sensitive meningioma [4].
2. Cyproterone acetate has a clear dose-dependent relationship with tumour growth in patients with meningioma [5]. Patients exposed to chlormadinone acetate and norgestrel acetate also have a higher risk of meningioma.
3. No studies have shown a definitive causal link or mechanism of action that use of HRT or hormonal contraception leads to the de novo development of meningioma [6-7].
4. In patients with meningioma there is a risk that both HRT and hormone contraception (mostly at higher doses of progesterone-containing compounds) may cause tumour growth or earlier recurrence. The evidence comes from a large French case-control study (18,061 operated cases vs. 90,305 controls) (8), an American study looking at over 10 million patients where propensity score matching was used to stratify groups and define the association with meningiomas (9) and a French population cohort study of 1,060,779 women (535,115 in the exposed group and 525,664 in the control group). *Compared to controls (i.e., no hormone exposure)* an increased incidence was noted with prolonged use of [8-10]:

- a. **Medrogestone** (oral)
- b. **Medroxyprogesterone acetate** injection (e.g., Depo-Provera)
- c. **Promegestone** (oral)
- d. **Nomegestrol acetate** (oral)
- e. **Chlormadinone acetate** (oral)
- f. **No increased risk** found with progesterone, dydrogesterone, or levonorgestrel intra-uterine systems

SBNS recommendation:

- Screening:

In patients who do not have a meningioma routine screening is not recommended prior starting HRT or hormonal contraception

- Avoidance:

1. Sporadic cranial meningioma (single, incidental, recurrent, residual, previously resected):

- a. Discuss the pros and cons of HRT or hormonal contraception balancing symptomatic benefit with the potential low risk of meningioma growth
- b. Explain that there is minimal/no material excess risk with oral, intravaginal, and percutaneous progesterone, as well as dydrogesterone and levonorgestrel intrauterine systems
- c. High dose progesterone-containing HRT or hormonal contraception pose a higher risk and alternatives should be considered e.g., levonorgestrel intra-uterine systems
- d. Patient with known meningioma considering IVF should make their IVF practitioner aware of their tumour diagnosis before commencing treatment
- e. Cyproterone acetate should be avoided as per the MHRA notice [11].

2. Non-sporadic (radiation-induced, NF2 etc.) and multiple meningioma:

- a. Strongly consider discontinuing all progestin containing medication due to the overall higher risk of meningioma growth. Alternatives treatments should be discussed with the GP or relevant healthcare professional (e.g., gynaecology for menorrhagia).

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