

Recent advances in the management of premature ovarian failure

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Welsh O&G Society
Swansea 2017

Recent advances in the management of
premature ovarian failure
insufficiency (POI)

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nomenclature

- Menopause before 40
 - “Premature Ovarian Insufficiency”
 - “Premature Menopause”

A spectrum: Overt, Biochemical, Occult (diminished ov reserve)

- Menopause between 40 to 45
 - “Early menopause”

Presentation

(Change in Menses pattern, Fertility)

menarche, puberty, COC, Pregnancy

(Estrogen deficiency symptoms)

Flushes, atrophic vaginitis

(low QoL score)

Examination

Biochemical

USS

In contrast to chromosomal, autoimmune or coexisting disorders Chemo/radio, Turners, Adrenal insufficiency (wt loss, abd pain, weakness, fatigue, anorexia), Hypothyroidism, vitiligo, myasthenia gravis, hypoparathyroidism, type 1 diabetes, fragile x (FMR1), developmental delay, deafness.

Diagnosis

- **Amenorrhea** not required , oligo or irregular >3/12
- **FSH level** Can be misleading, two occasions 6wks apart
- **Estrogen**
- **Symptoms** flushes, vag dryness, can be intermittent (25% of POI no symptoms)
- **P4 Test** for the spectrum
- **USS** endo thickness & AFC (75% may appear N)
- **AMH**
- **Karyotype , FMR1**, basic evaluation, particularly if <30/FH
- **Adrenal autoantibodies**, Thyroid & TSH antibodies
- **Other: DEXA, BhCG, Prolactin**
- **Early Diagnosis** Menstrual, bone health, Fertility, Emotional health, Coexisting disorders. The lack of proper diagnostic criteria for early stage POI, remains as a main problem.

Genetic Testing

Gene	Location	function
FMR1	Xq	Oocyte development & Number
SF1	11q	Maturation & Ov steroidogenesis
INHBA (inhibin α) #	2q	Folliculogenesis
LHR	2p	Foll growth & maturation
FHSR #	2p	Foll development
FOXL2	3q	Ovarian dev (undif granulose)
FOXO3a	6q	Foll activation
ER1 #	6q	Folliculogenesis
CYP19A1	15q	Ov differentiation
CXCL12	10q	GC migration
FMR2	Xq	Unknown
NOBOX	7q	Early folliculogenesis
DIAPH2	Xq	Foll development
MTHFR	1p	Folliculogenesis
LAMC1	1q	High expression during ovulation

Microdeletion
in X

Gene
Polymorphism

Depletion
vs
Dysfunction

<https://ukgtn.nhs.uk>

www.orpha.net

Menstrual

HT

Fertility

Bone health

Emotional health

- COC currently

- limited data to support particular regimens, simple, socially acceptable
- symptoms pill-free wk
- supra-physiological doses

- Estrogen currently

- transdermal preferred option adv: byP-hepatic metabolism & subsequent dec risk of ThEm
- E preparations

- + Progesterone

- MPA 10 for 12, Mirena (ongoing RCT)

- Cont comb/sequential

- no data
- complicated by unscheduled breakthrough bleeding

- Continuation with HT
 - 7% stop within 5years;
 - reassurance against the misperception surrounding HT in POI (No evidence of increased risk of breastCa)
- Non-hormonal
 - vasomotor serotonin reuptake inhibitors
 - no bisphosphonates if wish conception
 - no data supporting herbal/alternative therapy
- General lifestyle
 - supplement Ca & VitD, smoking, exercise

- Sexual well-being

- Low sexual satisfaction
- complex, T no sig diff in QoL, counselling

- Psychological

- Psychological distress high (regardless of HT) “traumatic”
- Depression, anxiety, reduced self-esteem, Neg self-image, overall life satisfaction.
- Counselling, support groups (daisynetwork.org.uk), psychologist.

- Fertility

- 50% intermittent (FSH up-regulated, dec LH: dec inappr luteinisation).
- 5-10% conceive spontaneously
- COC intermittent, Inconclusive : DHEA, GnRHa, CC
- Oocyte donation highest chance of conception (40-50%/cycle)
- Embryo donation, Surrogacy, Adoption
- Fertility preservation prior to Chemo/Radio (**NICE**); Oo / embryo / Ov tissue
- Inconclusive: Ovarian suppression prior to chemo
- Transposition & Shielding Ovarian tissue extremely sensitive, scattered radiation

- Long-term

- Life expectancy 2 years less (Menop over 55)
- CVD, osteoporosis, neurocognitive decline (verbalfluncy & visual memory)

- Future direction

- Much remains unknown
- Need for long-term studies (www.poiregistry.org)
- Standardisation of guidelines
- Interesting areas of research
 1. Identification of Oogonial stem cells (OSCs)
 2. Connected without nursing
 3. Cortical Ov tissue transplantation

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Thank You