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Saturday, June 10, 2017

8:30 - 9:25  WS #93: Optimising Fertility - Periconception Management
9:35 - 10:30  WS #105: Optimising Fertility - Periconception Management
(Repeated)
GPCME Rotorua
Optimising the periconception period

10th June 2017
Devashana Gupta
Mrs LM

- 28 year old
- 5 years of primary infertility
- Investigations in China- ?bilateral tubal occlusion on HSG.
- Normal menstrual cycles, normal BMI
- Normal pelvic USS
- RSA: reduced motility 28%
- What now? Why are my tubes blocked? Can I unblock them? Is IVF the only treatment I can undergo? What about my partners sperm?
WHO Semen Parameters 2010

- Developed using fertile men with partners TTC <12/12 as reference population
- Lower reference limit = 5th centile
- Volume = 1.5 ml
- Concentration = 15M/ml
- Total count* = 39M/ejaculate
- Total motility = 40%; progressive motility* = 32% (a+b)
- Morphology = 4% normal forms
- Vitality = 58% live
- Antisperm antibodies = <50%
- Leukocyte = <1
Tubal disease

• Types:
  • Congenital- rare, e.g. aplasia, segmental atresia, mucosal polyps.
  • Acquired- infection, SIN, tubal adhesion/occlusion and endometriosis.
  • Unknown - 50% due to subclinical Chlamydia. Recent evidence of Mycoplasma genitalium OR 2.43 for tubal infertility

• Impact:
  • Infertility
  • Obstruction to gametes
  • Increased ectopic pregnancies
  • Pelvic pain potentially if bilateral non communicating hydrosalphinx
  • Potential nidus for further infection if fluid present in tubes
Management

• Assessment: HSG/saline sonohystogram/HyCoSy or laparoscopy & dye
• Surgical versus IVF
• Surgical:
  • Reconstruction- distal* versus proximal disease, bilaterality, age, access to IVF
  • Distal disease- surgery >successful 75-90%. Options of fimbrioplasty versus neosalpingostomy
  • Proximal- success lower, risks of re-obstruction and perforation. Options of hysteroscopic or fluoroscopic cannulation or tubocornual reanastomosis
  • What of tubal ligation reversal?
• IVF has a shorter TTC but eventually achieve a similar pregnancy rate with time.
**Salpingectomy pre IVF**

- **Impact on fertility:**
  - leakage of hydrosalpingeal fluid
    - possible flush out effect
    - direct embryotoxicity
    - endometrial disruption & impairs endometrial receptivity (reduced LIF expression)
  - reduces sperm motility

- **Level I evidence for salpingectomy/occlusion pre IVF**
  - Large MA >6000 cycles showed halving of CPR and doubling of miscarriage rate with hydrosalphinx
  - Cochrane review 2010 OPR OR 2.14 with salpingectomy, occlusion not powered for OPR but increased CPR (Tubal occlusion- may increase potential for further surgery due to non patent obstruction)
### What do I offer and to whom?

<table>
<thead>
<tr>
<th>Surgery</th>
<th>IVF</th>
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<tbody>
<tr>
<td>Young</td>
<td>Cost if not public</td>
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<tr>
<td>Allows NC- cumulative conception</td>
<td>Co-existing male factor</td>
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<tr>
<td>Complementary to IVF</td>
<td>Proximal tubal disease</td>
</tr>
<tr>
<td>Cost if not publicly funded as 1st package</td>
<td>One pregnancy desired</td>
</tr>
<tr>
<td>Allows treatment of co-existing disease</td>
<td></td>
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<tr>
<td>Low AMH??</td>
<td></td>
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<tr>
<td>Distal disease</td>
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</table>
So Mrs LM?

- Recommend repeat RSA for partner- normal
- Wait listed for IVF after discussion of options —IVF versus surgery
- Discussion of assessment of tubal status re hydrosalpinges prior to commencement of IVF ?salpingectomy
- Other benefits of salpingectomy- possible reduction in risks of ovarian cancer
- Tubal occlusion- may increase potential for further surgery due to increased non patent obstruction
Lipiodol

- AKA ethiodized oil, is poppy seed oil
- Standard test until 40 years ago, now making a resurgence
- Effects: dislodging debris in fallopian tubes and flushing out mucous plugs. Also potential immunological effect on endometrium*. 
- Benefit lasts potentially 6/12 with majority of outcomes within 4/12
  
- Beneficial: women with unexplained infertility and mild endometriosis
- H2Oil study- OPR 40% versus 29%/ NNT=10
- Adverse events- theoretic intravasation with subsequent fat embolus
Miss CP

• 39 yr old
• Primary infertility of 8 years, AMH 5pmol/l
• Partner- obese, T2DM and hypertension
• Undergoing publicly funded IVF treatment
  • during ovarian stimulation found to have a large fibroid uterus.
• 4 oocytes→2 injected and 1 ET, none for freeze
• Unfortunately not pregnant
• What now? Proceed with second cycle? What of the fibroid?
Fibroids

• Formal USS assessment
  • large 15cm posterior intramural fibroid plus smaller subserosal fibroid.
  • Cavity distortion difficult to ascertain.
Fibroid classification

- Type 0 - pedunculated SM fibroid
- Type 1 - SM fibroid with <50% IM extension
- Type 2 - SM fibroid with >/=50% IM extension
- Type 3 - IM fibroid that contacts endometrium but 100% IM position
- Type 4 - Solely IM
- Type 5 - Subserosal with >50% IM location
- Type 6 - SS with < 50% IM location
- Type 7 - SS pedunculated
- Type 8 - other e.g. cervical
Uterine fibroids

• ACCEPT guidelines 2011
• Effect on fertility (Level 3 evidence)
  • SS don’t appear to have an effect
  • IM may be associated with reduced fertility and increased miscarriages
  • SM associated with reduced fertility and increased miscarriages
• Management of fibroids in infertile women
  • Hysteroscopic resection likely to improve fertility outcomes (level 2)
  • IM insufficient evidence to determine benefit (Level 2)
  • Fibroid size, number and location may impact on the usefulness of myomectomy
• Indications for myomectomy
  • Infertile woman with SM fibroid (level 2)
  • Infertile woman with symptomatic fibroids (level 4)
  • Previous multiple failed ART cycles with IM fibroids (level 4)
Uterine polyps

- Polyps may interfere with fertility but controversial
- Depends on the size and type of treatment
- CR 2015: OR 2.45 for clinical pregnancy with removal of endometrial polyp prior to IUI treatment
- Lass 1999- 2cm polyps trend to increased pregnancy loss
- Therefore, historically recommend removal of polyps >2-3cm if undergoing IUI/IVF
What of uterine septum's?

- Septate uterus: $\geq 1.5$cm int. indentation and external cleft $<1$cm
- Assess degree of septation: partial versus complete
- Associations such as vaginal septum, renal anomalies
- Poor blood supply of septum: therefore impaired implantation
- Fertility/pregnancy: recurrent miscarriage, preterm delivery, malpresentation
- Management: if no other cause found for infertility/miscarriage
- Benefit with resection: uncontrolled studies
Interesting fact!

- Uterine transplant with successful live birth in 2014 in Sweden
- Patient had MRKH syndrome
- Underwent IVF with 11 embryos frozen
- Uterine donation from menopausal friend
Miss CP?

- Discussion of evidence (moderate quality) of myomectomy before next cycle.
- Will be 40 before able to commence cycle. Partner lifestyle modification
- Referred for a myomectomy preceding next IVF cycle
- Risks of potential surgery including hysterectomy discussed

- Indications for myomectomy (ACCEPT)
  - Infertile woman with SM fibroid (level 2)
  - Infertile woman with symptomatic fibroid (level 4)
- UAE
  - Not recommended in women wishing to conceive until safety and effectiveness established
Male infertility

• Mrs JD, 38 yr old and Mr KL, 39 yr old
• PCOS with 3/3 criteria met
• Semen analysis- motility 12%, concentration 5.5 M/ml and morphology 3% normal forms.
• Benign history- no injuries/surgeries.
• Normal genital examination and general examination
• On leaving he mentions he has been on testosterone for a low libido!
Testosterone use in men

Indications:
• Androgen deficiency in men with pituitary/testicular disorders
• Androgen deficiency in men >40 with no disease
• Boys <18 with micropenis, constitutional delay of growth/puberty for pubertal induction
• Androgen deficiency- is a clinical diagnosis with a pathological basis confirmed by hormonal assays (2 * morning T <6nmol/l plus LH 1.5*normal)

Inappropriate use:
• Male infertility
• Sexual dysfunction
• Low energy
• Obesity
• Aging
• Osteoporosis without pathological hypogonadism
Mr KL?

- Cease testosterone use
- Discussed contraceptive effect of Testosterone
- Recommend hormone assay 6 weeks after cessation
- Assessment of cardiovascular status, follow up Hct and PSA
- Repeat RSA 6 months later- normal motility
- Another 6/12 later following OI with Letrozole
  pregnant!
Ms CN

- 32 yr old
- Recurrent pregnancy losses- G3P0M3
- Karyotype: balanced translocation of 14 for partner
- Referred for discussion of PGD/IVF
- Baseline lx: elevated TSH 3.9mIU/l, T4 normal
- All else normal
## Thyroid disorders

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<tr>
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<th>Hypothyroidism</th>
<th>Hyperthyroidism</th>
<th>Subclinical hypothyroidism</th>
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<tbody>
<tr>
<td><strong>TFT</strong></td>
<td>TSH-high FT4- low</td>
<td>TSH- low FT4- high</td>
<td>TSH- high * (? &gt; 2.5mIU/L) FT4 normal</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Menstrual irregularity</td>
<td>Irritability, disturbed sleep</td>
<td>Nil</td>
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<tr>
<td></td>
<td>Psychomotor retardation</td>
<td>Heat intolerance</td>
<td></td>
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<td></td>
<td>Cold intolerance</td>
<td>Palpitations</td>
<td></td>
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<tr>
<td><strong>Signs</strong></td>
<td>Bradycardia Delayed reflexes, dry skin</td>
<td>Tachycardia, warm skin Tremor, Goitre</td>
<td>Nil</td>
</tr>
<tr>
<td><strong>Impact on fertility</strong></td>
<td>Subtle effect on ovulation*, decr implantation, incr MR, PTB</td>
<td>Incr MR, PTB, PETR and maternal cardiac failure. Thyroid storm precipitated by stress e.g. labour</td>
<td>Maybe associated with adverse outcomes in TPO positive women e.g. recurrent miscarriages</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Thyroxine</td>
<td>PTU/Carbimazole</td>
<td>Controversial</td>
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Subclinical hypothyroidism

- Treatment is controversial
- Retrospective studies - improvement in obstetric outcomes with T4 Rx but not proven to modify long term neurological outcomes in children
- 2017 ATA new guidelines:
  - Insufficient data for/against Rx in TPO negative infertile women not undergoing ART
- ES recommendations:
  - T4 Rx in TPO pos/neg women as benefits outweigh risks
- Bottom line - probably best to treat:
  - If TSH >2.5mIU/l and infertile
  - Definitely if commencing ART
  - Definitely if >4.2mIU/l

TSH trimester specific guide:
T1 <2.5mIU/l
T2 and T3 <3mIU/l
Ms CN

- Commenced on Thyroxine 50mcg daily
- Repeat TFT a month later: TSH 2.9mIU/l
- IVF with PGD and successful pregnancy following euploid embryo transfer.
Miss LT

- 32 year old
- Recent diagnosis breast cancer, ER positive
- Planned for lumpectomy and SNB
- Referred for discussion of fertility preservation
- In a relationship for 6/12
Infertility after cancer treatment
Chemotherapy effects on ovaries

Chemotherapy effects
• no effect
• temporary ovarian failure (TOF) with apparent recovery
• permanent ovarian failure (POF)
• later onset premature ovarian failure (LO-POF)
Options for females

- Conservative approach
- GnRHa e.g. Zoladex during treatment
- Oocyte freezing (or IVM)
- Embryo freezing
- Ovarian tissue freezing
- Ovarian transposition
- FPR later in life
Miss LT

- Opted for oocyte freezing
- Protocol for fertility preservation is modified
- Try to maximise egg numbers, minimise harm and treatment burden
- AMH may not be available before commencement
- Random start cycle
- Agonist trigger
- Use of letrozole
- Studies show 15-20 oocytes need to be frozen for 1 successful LB (4% -12% per oocyte)
Thank you