OHSS: prediction, prevention and treatment

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Prediction
Prevention
Treatment

Clinically relevant OHSS
OHSS that requires hospitalisation

WHO grade III
Golan 1999 grade IV-V
Novotl 1997 "severe" or "lutea"
Risk 1999 grade B-C
Can we reliably predict OHSS?

Long GnRH-agonist protocol
De Angelis et al., 2004
E2 = 3,354 pg/ml
Sens + Spec = 85%

Long GnRH-agonist protocol
Papaplecosi et al., 2006
18 follicles >10 mm or E2 > 5,000 pg/ml
Sens = 83%
Spec = 84%

5/53 CASES OF SEVERE OHSS
STILL MISSED WITH THESE CRITERIA

AMH

Long GnRH-agonist protocol, n = 262
Lee et al., 2008; Sensitivity 90.5%, Specificity 61.1%
No reliable test to identify all OHSS risk patients

→ develop ovarian stimulation routines that are associated with a *per se* decreased risk of OHSS

→ but still need measures of OHSS prevention for individual patients, which are safe and efficacious, and can therefore be liberally utilized

How to prevent OHSS?

OHSS incidence reduction *efficacy*

- Natural cycle IVF  √  ?
- In vitro Maturation  √  ?
- Cycle cancellation  √  ---

Crude incidence of OHSS = 1.5%
A mild treatment strategy for in-vitro fertilisation: a randomised non-inferiority trial

<table>
<thead>
<tr>
<th>All treatment (n=180)</th>
<th>GnRH-antagonist daily (n=90)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of OHSS (%)</td>
<td>2.0 (1.5 - 2.5)</td>
<td>0.0004*</td>
</tr>
<tr>
<td>Median of FSH level (IU/L)</td>
<td>18.6 (16.5 - 20.8)</td>
<td>0.0004*</td>
</tr>
<tr>
<td>Complete of protocol (%)</td>
<td>96.7 (91.3 - 102.0)</td>
<td>0.0004*</td>
</tr>
<tr>
<td>Number of oocytes retrieved (n)</td>
<td>14.8 (13.4 - 16.2)</td>
<td>0.0004*</td>
</tr>
<tr>
<td>Median of estradiol level (ng/mL)</td>
<td>269 (244 - 301)</td>
<td>0.0004*</td>
</tr>
</tbody>
</table>

Gustofson et al., Hum Reprod 2006
Gustofson et al., Fertil Steril 2006

n= 85, coasting ~ 1.5 days
Ongoing pregnancy rate: ~ 60 %
Severe OHSS: 1.5 - 7.5 %

Novel concepts in OHSS prevention:
GnRH-antagonists

Novel concepts in Coasting

Incidence of OHSS = 1.4%
Heijnen et al., Lancet 2007; 369: 743–49
**Novel concepts in Coasting**

RCT: 192 patients

<table>
<thead>
<tr>
<th></th>
<th>Antagonist coasting</th>
<th>Conventional coasting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of coasting</td>
<td>1.74 ± 0.91</td>
<td>2.82 ± 0.97</td>
</tr>
<tr>
<td>No of oocytes</td>
<td>16.5 ± 7.6</td>
<td>14.06 ± 5.2</td>
</tr>
<tr>
<td>No of embryos</td>
<td>2.87 ± 1.2</td>
<td>2.21 ± 1.1</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>55.32%</td>
<td>47.92%</td>
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<tr>
<td></td>
<td>(N.S.)</td>
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</table>

No OHSS in both study groups

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**Novel concept: Luteal phase antagonist**

Report on 3 cases with early-onset OHSS

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**Novel concept: Luteal phase antagonist**

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Aboulghar et al., RBMonline 2007

Lainas et al., RBMonline 2007

Kolibianakis, personal communication
Does GnRH-agonist triggering prevent OHSS?

RCT

Observational study

OHSS III: RR with 95% confidence intervals (heterogeneity p = 0.90)

<table>
<thead>
<tr>
<th>Population</th>
<th>Study</th>
<th>Year</th>
<th>against</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>general</td>
<td>2005</td>
<td>0.90</td>
<td>2.02</td>
<td>0.10 - 0.40</td>
</tr>
<tr>
<td>OHSS</td>
<td>2006</td>
<td>0.75</td>
<td>1.63</td>
<td>0.15 - 0.93</td>
</tr>
<tr>
<td>OHSS vs. normal</td>
<td>2007</td>
<td>0.75</td>
<td>1.63</td>
<td>0.15 - 0.93</td>
</tr>
</tbody>
</table>

Update of: Griesinger et al., Hum Reprod update 2006
Novel concepts in treatment: Cabergolin

Background:

VEGF → VEGF R1 → Vascular fluid leakage

Cabergoline: Dopamine R agonist

RCT: placebo-controlled
Intervention: Cab 0.5 mg, day hCG → hCG+8
Patients: oocyte donors
Inclusion: > 20 oocytes retrieved

n=37 Cabergoline,
OHSS II: 7 (20%)
OHSS III: 4 (11.4%)
n=32 Placebo,
OHSS II: 14 (43.5%)
OHSS III: 6 (18.8%)
Novel treatment concepts: Renin-Angiotensin-system

- Alacepril™
- Candesartan Cilexetil ©
- ACE blocker
- Angiotensin receptor blocker

Report on 4 cases (abstract)
No ascites, no OHSS
No Hct elevation
Ando et al, Hum Reprod 2003

Report on 10 cases:
2 patients developed severe OHSS
Ata et al, in press

Novel treatment concepts: hCG antagonist

- hCG-antagonist
- LH/hCG receptor

- Competitive binding to LH receptor, but not stimulation (cAMP elevation)
- Reduced ovulation after PMSG stimulation
- Reduced vascular permeability

Vardhana et al., Fertil Steril (suppl) 2006