Recombinant FSH dosing during controlled ovarian stimulation in IVF treatment

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**Background**

During IVF treatment, recombinant FSH (rFSH) is used to induce multi-follicular growth (controlled ovarian stimulation; COS). Insufficient rFSH dose negatively impacts the number of oocytes retrieved, whereas excessive dose risks the potentially life-threatening complication ovarian hyperstimulation syndrome (OHSS). Hence, appropriate rFSH dosing is regarded as a key treatment decision affecting both the success and safety of IVF treatment.

Current dosing calculators for rFSH are derived to number of oocytes retrieved, however we investigated whether rFSH dosing can more accurately predict follicular growth.

**Aims**

- Evaluate pharmacokinetics of rFSH by assessing serum FSH level.
- Identify dose-response relationships between rFSH dose and follicular growth.
- Determine the impact that rFSH dose adjustment has on follicle growth and number of mature oocytes retrieved.

**Methods**

A single centre retrospective cohort study of 1,034 cycles (Jan 2012-Jan 2016) at Hammersmith IVF unit, where rFSH (GonalF) alone was used to induce follicular growth. Size of each individual follicle at each ultrasound scan and rFSH doses during COS were collated. Parametric groups were compared by ANOVA with post hoc Tukey’s and non-parametric data by Kruskall Wallis test with post hoc Dunn’s tests. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

**Results – Dose of GonalF adjusted for weight predicts serum FSH level**

**Figure 1**

![Figure 1](https://example.com/Figure1.png)

**Figure 1** Simple linear regression of serum FSH level (IU/L) after 4-5 days of GonalF by (A) Weight (kg); r²=0.108, p=0.0001; and by (B) BMI (kg/m²); r²=0.133, p=0.0001 (n=156).

**Results – Dose-response relationship between recombinant FSH dose and follicular growth**

**Figure 2**

![Figure 2](https://example.com/Figure2.png)

**Figure 2** Simple linear regression of serum FSH (IU/L) after 4-5 days of GonalF by (A) starting GonalF dose per kg (IU/kg); r²=0.352, p<0.0001; and by (B) starting GonalF dose per unit BMI (IU/kg/m²); r²=0.338, p<0.0001 (n=166).

**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting GonalF/kg (IU/kg)</td>
<td>0.058</td>
<td>0.02 to 0.095</td>
<td>0.003</td>
</tr>
<tr>
<td>Antral Follicle Count</td>
<td>-0.011</td>
<td>-0.013 to -0.008</td>
<td>0.0001</td>
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<tr>
<td>Pre-treatment screening FSH (IU/L)</td>
<td>-0.007</td>
<td>-0.023 to 0.008</td>
<td>0.36</td>
</tr>
<tr>
<td>Age</td>
<td>-0.009</td>
<td>-0.017 to -0.000</td>
<td>0.038</td>
</tr>
<tr>
<td>Constant</td>
<td>1.495</td>
<td>1.205 to 1.784</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**Conclusion**

- Recombinant FSH should be weight-adjusted.
- There is a dose-response relationship for starting GonalF dose at doses between 1.5 and 2.25 IU/kg to median follicle size after 5 days of treatment and to the proportion of antral follicles recruited.
- No further increased response beyond an rFSH dose of 2.25IU/kg
- Commencing COS with a sufficient starting dose of rFSH is advantageous reducing variability in follicle size and improving the number of mature oocytes retrieved.