Immobilisation versus immediate mobilisation after intra-uterine insemination; a randomised controlled trial

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Introduction

Unresolved issue: supine position or immediate mobilisation?

PICO-question

• Primair subfertiel paar
• Man 33 jaar; vrouw 34 jaar
• 26 maanden bezig
• OFO normaal (VCM 42 ml; PCT normaal)
• Diagnose: subfertilité e.c.i.
• Behandelplan: IUI met milde stimulatie
• 10 minuten blijven liggen of opstaan
A randomized study of the effect of 10 minutes of bed rest after intrauterine insemination

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Aim: To evaluate the effects of 10 minutes of bed rest after intrauterine insemination (IUI) on the pregnancy rate.

Design: Prospective randomized study.

Setting: University setting.

Participants: 100 patients undergoing IUI were randomized into two groups: Group A (bed rest for 10 minutes after IUI) and Group B (no bed rest after IUI).

Intervention: Patients in Group A were instructed to remain supine for 10 minutes after IUI, while patients in Group B were allowed to assume their usual position immediately after IUI.

Main Outcome Measures: Pregnancy rates were compared between the two groups.

Results: Of the 100 patients, 90 in Group A and 90 in Group B were eligible for analysis. There were 21 pregnancies in Group A (23.3%) and 15 pregnancies in Group B (16.7%). The difference was statistically significant (p = 0.04). The mean age of the patients in Group A was 36.7 years, and in Group B, it was 37.1 years (p = 0.25).

Conclusion: A 10-minute period of supine rest after IUI has a positive effect on the pregnancy rate. It is recommended to instruct patients to remain supine for 10 minutes after IUI to optimize pregnancy chances.

<table>
<thead>
<tr>
<th></th>
<th>Pregnant</th>
<th>Not pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>16</td>
<td>104</td>
</tr>
<tr>
<td>Move</td>
<td>4</td>
<td>86</td>
</tr>
</tbody>
</table>

NNT = 1 / (13.3% - 4.4%) = 11 cycli blijven liggen voor 1 extra zwangerschap
95% betrouwbaarheidsinterval 6 tot 68

Objective

- Assess the effect of 15 minutes of immobilisation versus immediate mobilisation after Intra Uterine Insemination

Study design

Multi centre trial
7 clinics
Study design

• Inclusion criteria:
  – All patients with an indication for IUI
  • With fresh or cryo-preserved sperm (donor or husband’s)
  • With or without controlled ovarian hyperstimulation
  • Anovulatory women: after failed ovulation induction
  – At least one patent tube
  – At least 18 years of age

Study design

• All couples underwent basal fertility work up
  – Diagnosis male factor subfertility: TMC < 10 *10⁶/mL
  – Cervical factor: no progressive spermatozoa in (at least one well-timed) PCT (TMC >10 *10⁶/ml)
  – Unexplained subfertility: PCT positive, progressive and TMC >10 *10⁶/ml

Study design

• Informed consent obtained
• Randomisation by computer
  – Before the first insemination
  – Stratification: female age and centre
• Parallel design
• Three consecutive cycles in supine position after IUI or three cycles immediate mobilisation
Study design

• Procedure IUI:
  – COH with:
    • Clomiphene citrate
    • r/uFSH
  – No COH
• Timing of ovulation with 5000 IU HCG
• Insemination of 0.3-1.0 mL of processed spermatozoa
• Insemination in lithotomy position with Trendelenburg tilt

Validity

• Randomisation
• Blinding of allocation (concealment)
• Blinding of endpoint
  • Patienten / doctors / observers
• Follow-up
• Intention to treat analysis

Comparable groups?
Randomisation

- Envelopes
- Computers
- Webbased
- Telephone
  - Independent party
- Concealment
Follow up

• 3 cycles of IUI (max. of 4 months) or
• ongoing pregnancy (12 weeks gestation)

Outcome measures

• Primary outcome measure
  – Ongoing pregnancy rate per couple

• Secondary outcome measures
  – Live birth rate
  – Pregnancy rate per cycle
  – Multiple pregnancies
  – Miscarriages
  – Ectopic pregnancies
  – Biochemical pregnancies
Power calculation

- Testing the 0-hypothesis
- Alpha-error beta-error
- Equivalence study
- Lasagna’s law

Increase of 4% per cycle (= 12% per couple),
- A dropout rate of 10%
- 185 couples per arm
  (one-sided test, α-error of 0.05, β-error of 0.20).
Analysis

• Intention to treat principle
• Primary and secondary outcome measures expressed in PR per couple and RR with 95% CI

Logistics

• Research nurses
• Data collection

Results

Trial profile
Results

Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>15 Minutes of immobilisation (n=199)</th>
<th>Immediate mobilisation (n=192)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female age (years)</td>
<td>33.9 ± 3.8</td>
<td>33.3 ± 3.9</td>
</tr>
<tr>
<td>Duration of subfertility (years)</td>
<td>2.7 ± 1.4</td>
<td>2.7 ± 2.3</td>
</tr>
<tr>
<td>Primary subfertility</td>
<td>158 (79)</td>
<td>158 (77)</td>
</tr>
<tr>
<td>Cause of subfertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unexplained</td>
<td>118 (59)</td>
<td>109 (56)</td>
</tr>
<tr>
<td>Cervical factor</td>
<td>58 (29)</td>
<td>63 (33)</td>
</tr>
<tr>
<td>Poor semen quality²</td>
<td>23 (12)</td>
<td>24 (13)</td>
</tr>
<tr>
<td>One-sided tubal pathology</td>
<td>21 (11)</td>
<td>20 (10)</td>
</tr>
<tr>
<td>Normal</td>
<td>118 (60)</td>
<td>124 (65)</td>
</tr>
<tr>
<td>Gris</td>
<td>1 (1)</td>
<td>0</td>
</tr>
</tbody>
</table>

Values between (..) are percentages

*Values are means ± SD

²TMC <10⁶/ml

Results

Outcome measures, intention to treat analysis

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>15 min. immobilisation (n=199)</th>
<th>Controls (n=192)</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing pregnancy (%)</td>
<td>54 (27)*</td>
<td>34 (18)**</td>
<td>1.5 (1.1-2.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Live birth (%)¹</td>
<td>53 (27)</td>
<td>32 (17)</td>
<td>1.6 (1.1-2.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Twin pregnancy²</td>
<td>3 (6)</td>
<td>1 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriages (%)</td>
<td>14 (7)</td>
<td>17 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ectopic pregnancy (%)</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemical pregnancy (%)</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of cycles performed</td>
<td>2.4</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*4 spontaneous pregnancies, 1 after escape IVF

**5 spontaneous pregnancies

¹16 couples still pregnant, considered as live birth in analysis

²Calculated per ongoing pregnancy

Results

Outcome measures, survival curve

[Graph showing survival curve with labeled axes and data points]

log-rank test, p = 0.026
Conclusions

- Immobilisation after IUI leads to increased ongoing pregnancy rates
- Immobilisation should be incorporated in IUI guidelines