Is the fallopian tube better than the uterus?

Evidence on intrauterine insemination vs fallopian sperm perfusion

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Norway
Thanks to my friend and colleague
Jarl Kahn
Thanks to my friend and colleague Jarl Kahn

I want to flush the tubes with sperm. This will increase the chance that the egg and the sperm meet...!!

Ok..?
Fallopian tube perfusion - FSP

- End of the 80’ties
  - “We want to flush the tubes with sperm”

- Volumetric study on volunteers to be sterilised.
  - The uterus perfused with using an IV-pump set at 0,5ml/min
  - Fluid passed out of the distal end of the tubes after 0,5-1,8ml was perfused.

- “let’s use 4ml inseminate..”

Kahn et al Human Reprod. 7 (suppl 1), 19-24, 1992
FSP – first results

- Tested on patients with different infertility diagnosis
  - 139 couples, 239 cycles,
  - 32 pregnancies (23% / 13.4%)

- “Seems good in Unexplained infertility
  - (49% / 27%)”

- “Not good result where the semen quality is reduced (5.2%/3.0%)”

Kahn et al Human Reprod. 7 (suppl 1), 19-24, 1992
FSP – first results

• ”Not do good with reduced semen quality”

• The sperm was (is) prepared with direct swim-up or just centrifugation and wash

• We aim(ed) at 10 million motile sperm in the inseminate
FSP vs. semen quality

FSP better than IUI?

- A Prospective randomised multi-centre study
  - 60 couples randomised
  - FSP group 30 women, 52 cycles
  - IUI group 28 women, 51 cycles

Kahn et al. Human Reprod., 8, 890-894, 1993
FSP – how to do it?

- **Fanchin et al.**
  - A new system for fallopian tube sperm perfusion leads to pregnancy rates twice as high as standard intrauterine insemination
  - *Fertil Steril.* 64, 505-510, 1995
  - *A special device ”The FAST System ©”*

- **Mamas, L**
  - Higher pregnancy rates with a simple method for fallopian tube sperm perfusion, using the cervical clamp double nut bivalve speculum in the treatment of unexplained infertility: a prospective randomised study,
  - *”The DNB-Speculum©”*

- **Ricci et al**
  - A simple method for fallopian tube sperm perfusion using a blocking device in the treatment of unexplained infertility.
  - *Cervix adaptor, bivalve speculum, forceps*
FSP – how to do it?

• The different variants of FSP might well generate different results

• This is unknown and untested

• May contribute to the variations in results obtained
FSP – our results

- FSP in "Unexplained infertility"
- Donor insemination with frozen semen (Cryos, Denmark)
FSP with husbands semen
All indications

- Our data from 1988 to 2002

- 1340 started cycles
  - 221 cancelled cycles
    - 95 cycles to IVF (doing good)

- 1005 inseminations

- 142 pregnancies (14.1%)
- 112 deliveries (11.1%)
  - 5 sets of twins (4.5%)
  - 1 set of triplets (0.9%)
FSP with frozen donor semen

• Our data from 1990 to 2002
• 1316 started cycles
  – 116 cancelled cycles
    • Donor IVF not allowed

• 1200 inseminations

• 333 pregnancies (27.8%)
• 226 deliveries (18.8%)
  – 36 sets of twins (15.9%)
FSP – how many cycles?

• In our hands
  
  – the pregnancy rate drops after 3-4 cycles both in Unexplained infertility and in Donor insemination
  
  – We advocate not more than 3 cycles in Unexplained infertility
FSP vs. IUI
What’s best?

• Meta-analysis
  – An exercise on its own..
  —..😊
FSP – meta-analysis
The first one...

Trout & Kemmann. Fertil Steril. 71, 881-885, 1999
Cantineau AEP, Cohlen BJ, Al-Inany H, Heineman MJ.

Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Analysis 01.02.  Comparison 01 Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 02 pregnancy rate per couple for non tubal subfertility

Review:  Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility
Comparison:  01 Intrauterine insemination versus fallopian tube sperm perfusion
Outcome:  02 pregnancy rate per couple for non tubal subfertility

<table>
<thead>
<tr>
<th>Study</th>
<th>FSP</th>
<th>IUI</th>
<th>Odds Ratio (Fixed) 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gregoriou 1995</td>
<td>11/30</td>
<td>12/30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kahn 1993</td>
<td>14/30</td>
<td>5/28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuojua-Huttunen 1997</td>
<td>4/50</td>
<td>10/50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pireti 1999</td>
<td>33/46</td>
<td>17/49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ricci 2001</td>
<td>14/33</td>
<td>5/32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>237</td>
<td>237</td>
<td></td>
<td>100.0</td>
<td>1.85 [1.23, 2.79]</td>
</tr>
</tbody>
</table>

Total events: 85 (FSP), 57 (IUI)
Test for heterogeneity chi-square = 17.63 df=5 p=0.003 I^2 = 71.6%
Test for overall effect z=2.94 p=0.003

Cochrane Database of Systematic Reviews 2004
Cantineau AEP, Cohlen BJ, Al-Inany H, Heineman MJ.
Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Analysis 01.03. Comparison 01 Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 03
Subgroup: pregnancy rate per couple for unexplained subfertility

Review: Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility
Comparison: 01 Intrauterine insemination versus fallopian tube sperm perfusion
Outcome: 03 Subgroup: pregnancy rate per couple for unexplained subfertility

<table>
<thead>
<tr>
<th>Study</th>
<th>FSP n/N</th>
<th>IUI n/N</th>
<th>Odds Ratio (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Odds Ratio (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gregoriou 1995</td>
<td>11/30</td>
<td>12/30</td>
<td></td>
<td>42.4</td>
<td>0.07 [ 0.31, 2.46 ]</td>
</tr>
<tr>
<td>Kohn 1993</td>
<td>14/30</td>
<td>5/28</td>
<td></td>
<td>15.4</td>
<td>4.03 [ 1.21, 13.42 ]</td>
</tr>
<tr>
<td>Phetl 1999</td>
<td>33/46</td>
<td>17/49</td>
<td></td>
<td>25.9</td>
<td>4.78 [ 2.00, 11.41 ]</td>
</tr>
<tr>
<td>Ricci 2001</td>
<td>14/33</td>
<td>5/32</td>
<td></td>
<td>16.3</td>
<td>3.98 [ 1.23, 12.92 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>139</td>
<td>139</td>
<td></td>
<td>100.0</td>
<td>2.88 [ 1.73, 4.78 ]</td>
</tr>
</tbody>
</table>

Total events: 72 (FSP), 39 (IUI)
Test for heterogeneity chi-square=6.97 df=3 p=0.071 P=57.0%  
Test for overall effect z=4.08 p=0.00005

Cochrane Database of Systematic Reviews 2004
Cantineau AEP, Cohlen BJ, Al-Inany H, Heineman MJ.

Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility.

• “There is some evidence from subgroup analysis that FSP gives rise to higher pregnancy rates in couples with unexplained subfertility.”

Cochrane Database of Systematic Reviews 2004
• “A meta-analysis of five RCTs (number of patients in trials uncertain, 610 cycles) comparing fallopian sperm perfusion to IUI in women with various causes of infertility found that fallopian sperm perfusion improved pregnancy rates only in women with unexplained infertility who underwent controlled ovarian stimulation with gonadotrophin/insemination protocols (OR 1.9, 95% CI 1.2 to 3). [Evidence level 1a]”
Meta - analysis

- Recent Cochrane Review 2009
Cantineau AEP, Cohlen BJ, Heineman MJ.

‘Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility.

### Analysis 1.2. Comparison I Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 2 pregnancy rate per couple for non tubal subfertility.

**Review:** Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility

**Comparison:** I Intrauterine insemination versus fallopian tube sperm perfusion

**Outcomes:** 2 pregnancy rate per couple for non tubal subfertility

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>FSP</th>
<th>IUI</th>
<th>Odds Ratio M-HFixed95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-HFixed95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bianchi &amp; 2004</td>
<td>1/22</td>
<td>8/34</td>
<td></td>
<td>125 %</td>
<td>0.15 [ 0.02, 1.44 ]</td>
</tr>
<tr>
<td>Fi Sadek 1998</td>
<td>9/48</td>
<td>8/48</td>
<td></td>
<td>13.6 %</td>
<td>1.15 [ 0.40, 3.30 ]</td>
</tr>
<tr>
<td>Gregoriou 1995</td>
<td>11/30</td>
<td>12/30</td>
<td></td>
<td>15.9 %</td>
<td>0.87 [ 0.31, 2.46 ]</td>
</tr>
<tr>
<td>Kahn 1992</td>
<td>14/10</td>
<td>5/28</td>
<td></td>
<td>5.8 %</td>
<td>4.03 [ 1.21, 13.42 ]</td>
</tr>
<tr>
<td>Ng 2003</td>
<td>17/30</td>
<td>11/30</td>
<td></td>
<td>10.0 %</td>
<td>2.26 [ 0.86, 6.36 ]</td>
</tr>
<tr>
<td>Nugeja 1997</td>
<td>4/50</td>
<td>10/50</td>
<td></td>
<td>19.2 %</td>
<td>0.25 [ 0.10, 1.20 ]</td>
</tr>
<tr>
<td>Papier 1998</td>
<td>5/50</td>
<td>9/50</td>
<td></td>
<td>16.9 %</td>
<td>0.51 [ 0.16, 1.63 ]</td>
</tr>
<tr>
<td>Rizzi 2001</td>
<td>14/10</td>
<td>5/22</td>
<td></td>
<td>6.1 %</td>
<td>3.79 [ 1.23, 12.92 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>293</strong></td>
<td><strong>302</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>1.17 [ 0.79, 1.71 ]</strong></td>
</tr>
</tbody>
</table>

Total events: 75 (FSP), 68 (IUI)

Heterogeneity: Ch² = 19.11, df = 7 (P = 0.01); I² = 63%

Test for overall effect: Z = 0.79 (P = 0.43)

Cochrane Database of Systematic Reviews 2009
Cantineau AEP, Cohlen BJ, Heineman MJ.

Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility.

Figure 4. Forest plot of comparison: Intrauterine insemination versus fallopian tube sperm perfusion, outcome: 1.3 Subgroup: pregnancy rate per couple for unexplained subfertility.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>FSP Events</th>
<th>Total Events</th>
<th>III Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biacchiardi 2004</td>
<td>1</td>
<td>22</td>
<td>8</td>
<td>34</td>
<td>31.1%</td>
<td>0.15 [0.02, 1.34]</td>
<td></td>
</tr>
<tr>
<td>Gregoriou 1995</td>
<td>11</td>
<td>30</td>
<td>12</td>
<td>30</td>
<td>39.4%</td>
<td>0.87 [0.31, 2.46]</td>
<td></td>
</tr>
<tr>
<td>Kahn 1993</td>
<td>14</td>
<td>30</td>
<td>5</td>
<td>28</td>
<td>14.3%</td>
<td>4.03 [1.21, 13.42]</td>
<td></td>
</tr>
<tr>
<td>Ricci 2001</td>
<td>14</td>
<td>33</td>
<td>5</td>
<td>32</td>
<td>15.2%</td>
<td>3.98 [1.23, 12.92]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>115</strong></td>
<td><strong>124</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1.57 [0.89, 2.76]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 40, 30

Heterogeneity: Chi² = 10.42, df = 3 (P = 0.02); I² = 71%

Test for overall effect: Z = 1.57 (P = 0.12)
Cantineau AEP, Cohlen BJ, Heineman MJ.
Intra-uterine insemination versus fallopian tubesperm perfusion for non-tubal infertility. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD001502. DOI:

• “Implications for practice

• There is no evidence that FSP results in higher pregnancy rates in couples suffering from non-tubal subfertility than with IUI.

• This conclusion is based on eight studies involving a total of 595 couples. As a result no advice can be given, based on the meta analysis on the optimal treatment of non-tubal subfertility. We advise, therefore, familiarity with one procedure since knowledge and routine use of one technique is possibly of more importance than the technique itself.”
**FSP or IUI?**

- **Currently there is not sufficient evidence to suggests that FSP is better than IUI.**

- **Indication:**
  - ✓ *Unexplained infertility*
  - ? Reduced semen quality
    - The Gothenburg data
  - ? Endometriosis,
  - ? Cervical,
  - ? Ovulation disorders

- **There might be an effect of the way FSP is practically done**
  - Catheters, speculums, forceps….
  - Unknown which variant is the best…and if a certain variant consistently will give better results tat traditional IUI