New Developments in the IVF-Lab and their Impact on the Patient

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X. Turkish German Gynecology Congress
Antalya, 30.4.–4.5.2014
FRAUENKLINIK DER MEDIZINISCHEN HOCHSCHULE HANNOVER

Erfolgsrate nach Extrakorporaler Befruchtung

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Follikelpunktionen</td>
<td>25</td>
<td>56</td>
<td>53</td>
<td>130</td>
</tr>
<tr>
<td>Embryotransfers</td>
<td>5</td>
<td>20</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td>Schwangerschaften</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>14</td>
</tr>
</tbody>
</table>

30 %  20 %
Medizinische Hochschule
Hannover, 1984
## German IVF Registry

<table>
<thead>
<tr>
<th>Year</th>
<th>IVF Foll. punct.</th>
<th>IVF Pregn. rate</th>
<th>ICSI Foll. punct.</th>
<th>ICSI Pregn. rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>9927</td>
<td>27.39 %</td>
<td>25051</td>
<td>26.46 %</td>
</tr>
<tr>
<td>2009</td>
<td>9882</td>
<td>26.87 %</td>
<td>31289</td>
<td>27.36 %</td>
</tr>
<tr>
<td>2012</td>
<td>9237</td>
<td>26.89 %</td>
<td>31340</td>
<td>26.31 %</td>
</tr>
</tbody>
</table>
New developments in the IVF-Lab

Is it all a matter of selection?

Sperm selection
- IMSI
- PICSI

Embryo selection
- Blastocyst culture
- Quality Mixed Embryo Transfer

Endometrium selection
- Scratching
- Seminalplasma-Flushing
IMSI

Intracytoplasmatic Morphologically-selected Sperm Injection
Objective: To retrospectively evaluate whether sperm vacuoles influence clinical results, with a particular focus on 101 intracytoplasmic morphologically selected sperm injection (ICSI) cycles.

Setting: A medical center.

Patient(s): A total of 101 patients with at least two failed intracytoplasmic sperm injection (ICSI) morphology cycles were included in this study.

Intervention(s): Patients were divided into two groups according to sperm morphology and vacuole presence: Group A with good quality spermatozoa (type I and/or type II spermatozoa; n = 63 patients) and Group B with poor quality spermatozoa (type III and/or IV spermatozoa; n = 38 patients).

Main Outcome Measure(s): Fertilization rate, embryo quality, pregnancy, implantation, and live birth outcomes.

Result(s): No statistically significant differences were observed between Groups A and B with regards to fertilization rate and embryo quality. However, the “late” outcomes (pregnancy, live birth, statistically significantly higher in Group A.

Conclusion(s): These results confirm a correlation between sperm vacuoles and a negative ICSI outcome, suggesting that sperm vacuoles are related to the late paternal effect. (Fertil Steril 2013;100:379-85. © 2013 by American Society for Reproductive Medicine.)

Key Words: Clinical outcomes, intracytoplasmic, ICSI, live birth rate, morphologically selected sperm injection, vacuoles

Discussion: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/greece-sperm-vacuoles-imsi-live-birth-rate/
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Endometrium selection
Scratching
Seminalplasma-Flushing
Acrosome-Reaction

Schill Lab.med. 9 (1985) 63
Experiences with sperm selection by hyaluronic acid coated petri dishes (PICS1) in an ART program
N. Saymé, K. Sollmann, D.H.A. Maas, T. Krebs
ASRM 2013, Boston

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Fertilization rate</th>
<th>Embryo Quality</th>
<th>Pregnancy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICSI</td>
<td>PICS1</td>
<td>p</td>
</tr>
<tr>
<td>All samples</td>
<td>73,50%</td>
<td>73,86%</td>
<td>0,912</td>
</tr>
<tr>
<td>Normospermic</td>
<td>71,16%</td>
<td>64,20%</td>
<td>0,464</td>
</tr>
<tr>
<td>Oligospermic</td>
<td>68,47%</td>
<td>63,88%</td>
<td>0,546</td>
</tr>
<tr>
<td>Asthenospermic</td>
<td>74,96%</td>
<td>75,88%</td>
<td>0,833</td>
</tr>
<tr>
<td>Teratospermic</td>
<td>72,43%</td>
<td>74,50%</td>
<td>0,630</td>
</tr>
</tbody>
</table>
HBA

The sperm-Hyaluronan Binding Assay

HBA is designed to provide a qualitative assessment of sperm quality, maturity, and fertilizing potential.

- HBA provides a rapid assessment of sperm quality, maturity, and structural integrity.
- Correlations with fertility outcomes and morphology assessments.

Simple, objective, and rapid assessment (<60 seconds)

![Clinical Pregnancy Rate (CPR) chart](chart.png)

- All n=482
- F-HB >65% n=357
- F-HB ≤65% n=121
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STANDARD-CULTURE

Embryotransfer on day 2 in a (2-)4-(8-)cell-stage

LONGTERM-/BLASTOCYST-CULTURE

Embryotransfer on day 5 in the blastocyst-stage
## Pregnancy rates after Embryotransfer on Day 2/3 versus Day 4/5

<table>
<thead>
<tr>
<th>age</th>
<th>Day 2/3</th>
<th>Day 4/5</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>40.5 %</td>
<td>55.9 %</td>
</tr>
<tr>
<td>35-40</td>
<td>26.9 %</td>
<td>44.7 %</td>
</tr>
<tr>
<td>&gt;41</td>
<td>12.1 %</td>
<td>21.2 %</td>
</tr>
<tr>
<td>Total</td>
<td>28.4 %</td>
<td>46.8 %</td>
</tr>
</tbody>
</table>

2013 (Jan-Dec) 582 pat.
2014 (Jan-Mar) 138 pat.
Kinderwunschzentrum Ulm/Germany

I. El-Danasouri pers. comm 2014
New developments in the IVF-Lab

*Is it all a matter of selection?*

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**Endometrium selection**
- Scratching
- Seminalplasma-Flushing
Quality mixed embryo transfer

**Embryo scoring:**

**Morphology**

- **Grade A:** regular cleavage, no fragmentation
- **Grade D:** irregular cleavage, highly fragmented

**In-phase cleavage stages**

- Day 2: 4 cells
- Day 3: 8 cells
- Day 4: morula
- Day 5: blastocyst

I. El-Danasouri et al., pers.comm. 2014
Quality mixed embryo transfer

**Embryo scoring**

**Good:** Grade A + B  
Cleavage stages in phase or faster

**Poor:** Grade C + D  
Cleavage stages slowlier and out of phase

I. El-Danasouri et al., pers.comm. 2014
Quality mixed embryo transfer

785 patients at the age of $\leq$ 35 yrs. with transfer of one or two embryos

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Embryos</th>
<th>No. of Patients</th>
<th>Age (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>1 embryo</td>
<td>55 pat</td>
<td>31.8 ± 2.7 yrs</td>
</tr>
<tr>
<td>G+G</td>
<td>2 embryos</td>
<td>323 pat</td>
<td>32.0 ± 2.0 yrs</td>
</tr>
<tr>
<td>G+P</td>
<td>2 embryos</td>
<td>236 pat</td>
<td>32.6 ± 2.6 yrs</td>
</tr>
<tr>
<td>P+P</td>
<td>2 embryos</td>
<td>126 pat</td>
<td>33.1 ± 2.9 yrs</td>
</tr>
<tr>
<td>P</td>
<td>1 embryo</td>
<td>45 pat</td>
<td>32.6 ± 1.6 yrs</td>
</tr>
</tbody>
</table>

Kinderwunschzentrum Stuttgart, Germany, and RISEL-One Day Medical Center, Rome, Italy

I. El-Danasouri et al., pers.comm. 2014
Quality mixed embryo transfer

Pregnancy per ET %

I. El-Danasouri et al., pers.comm. 2014
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- Endometrium selection
  - Scratching
  - Seminalplasma-Flushing
NK-cells invade into the endometrium after ovulation until week 20 of pregnancy. They are regarded responsible (besides destroying virus-infected and tumouros cells) for *inducing vascular growth and immunological tolerance*.

Present therapeutic studies:

- **Inducing** the NK-cell number by
  - Endometrial scratching
  - G-CSF-injections
  - seminal plasma flushing

- **Reducing** the NK-cell-number by
  - intra venous infusions of lipid-preparations (omega-3/-6-fatty acids)

U. Markert, Jena, 2014
Pregnancy rate after insemination in the bovine with and without flushing the vagina/cervix with seminal plasma or culture medium as placebo.

M. Scherhoff, School of Veterinary Medicine, Hannover, 2012
Thank you for your attention!
New developments in the IVF-Lab

Is it all a matter of selection?

Sperm-selection
- IMSI
- PICSI

Embryo-selection
- Blastocyst culture
- Micro Vibration
- Mixed Embryo Transfer

Endometrium Stimulation
- Scratching
- Seminalplasma-Flushing
„Rüttler“
(„shaker“)

Three-dimensional vibration at 56 Hz delivered over 5 sec. every hour.
## Micro vibration

<table>
<thead>
<tr>
<th></th>
<th>Micro vibration (1–4 cell group-culture) 244 pat.</th>
<th>Static culture (single cell-culture) 291 pat.</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilization rate</td>
<td>82.1%</td>
<td>78.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>41.9%</td>
<td>35.5%</td>
<td>0.043</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>46.7%</td>
<td>43.3%</td>
<td>0.427</td>
</tr>
</tbody>
</table>

Kinderwunschzentrum Ulm and Kinderwunschzentrum Stuttgart

I. El-Danasouri et al., pers. comm. 2014