IMPACT OF PATERNAL AGE, EJACULATORY ABSTINENCE LENGTH AND SEMEN QUALITY ON THE OUTCOMES OF INTRACYTOPLASMIC SPERM INJECTION (ICSI) IN AN EGG-SHARING DONATION PROGRAM

Amanda Setti¹,², Daniela Paes de Almeida Ferreira Braga¹,², Bianca Zanetti², Livia Vingris¹; Assumpto Iaconelli Jr.¹, Edson Borges Jr.¹,²
INTRODUCTION

Infertility: 15% of the couples

Male factor

Others

Male partner factors → IVF

Most of the existing literature focuses on female infertility or on the fertility of both partners.
INTRODUCTION

Haploid genome

Gamete fusion

Gamete cleavage

Epigenetic regulation of embryogenesis
INTRODUCTION

Concerns about the contribution of the male factor to IVF outcomes

ICSI improve outcomes over conventional IVF for male factor infertility

Molecular Biology of the Cell, 4th ed.
INTRODUCTION

Sperm activation

Cortical granule release

Acrosome Reaction

Cumulus Dispersal and Penetration through ZP

Male gamete entrance

Binding to zona pelucida

Motility Hyper-activation

Capacitation

Molecular Biology of the Cell, 4th edition
INTRODUCTION

Men produce sperm through the entire life.

Recently, the potential role of paternal age has been investigated with conflicting results.

Molecular Biology of the Cell, 4th edition
The same is true for impact of abnormal sperm parameters on embryo implantation.
INTRODUCTION

The same lack of consensus is noted when it concerns the ejaculatory abstinence length

Recomendations for EA

1. Effect of EA on seminal parameters and sperm quality
2. Effect of EA on embryo development and implantation

The scientific evidences behind these recommendations are limited
OBJECTIVE

To evaluate the effect of paternal age, ejaculatory abstinence length and semen quality on ICSI outcomes in recipients’ cycles in an egg-sharing donation program
MATERIALS AND METHODS

• STUDY DESIGN

Historical cohort study

Between January/2015 and May/2017

Egg-sharing donation program

268 oocyte donor cycles (19-35 y-old)

427 oocyte recipient cycles (26-59 y-old)

Paternal Factors

General Mixed Models

Post-hoc power for the sample size: 95.7%.
MATERIALS AND METHODS

Predictive variables
- Paternal age
- Ejaculatory abstinence length
- Sperm count
- Progressive sperm motility
- Total motile sperm count

Response variables
- Fertilization rate
- High-quality embryos rate on D3
- Normal embryo development rate on D3
- Blastocyst development rate
- High-quality blastocysts rate
- Implantation rate
- Pregnancy rate
Controlled Ovarian Stimulation

MATERIALS AND METHODS

GnRH Antagonist
Recombinant FSH
Recombinant hCG

Ovum Pickup

E2

Menses
MATERIALS AND METHODS

Incubation, denudation and nuclear maturation evaluation

ICSI performed after denudation for donors or 3 hours after warming for recipients

Embryo culture until day 5

One or two blastocysts transferred
MATERIALS AND METHODS

Vitrification and the warming: Cryotop method

Semen samples were evaluated according to the threshold values established by the WHO in 2010

Sperm preparation: 2-layered density gradient centrifugation technique
MATERIALS AND METHODS

• EMBRYO MORPHOLOGY
## RESULTS

### Association between paternal age and ICSI outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Paternal Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>-0.276</td>
</tr>
<tr>
<td>High-quality embryos rate on D3</td>
<td>-0.040</td>
</tr>
<tr>
<td>Normal embryo development rate on D3</td>
<td>-2.750</td>
</tr>
<tr>
<td>Blastocyst development rate</td>
<td>-0.070</td>
</tr>
<tr>
<td>High-quality blastocysts rate</td>
<td>-44.058</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>-0.060</td>
</tr>
<tr>
<td>Pregnancy chance</td>
<td>Exp(B): 0.664</td>
</tr>
</tbody>
</table>
## RESULTS

### Association between ejaculatory abstinence length and ICSI outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Ejaculatory Abstinence Length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>-0.083</td>
</tr>
<tr>
<td><strong>High-quality embryos rate on D3</strong></td>
<td>-0.003</td>
</tr>
<tr>
<td><strong>Normal embryo development rate on D3</strong></td>
<td>-0.300</td>
</tr>
<tr>
<td><strong>Blastocyst development rate</strong></td>
<td>-0.589</td>
</tr>
<tr>
<td>High-quality blastocysts rate</td>
<td>13.812</td>
</tr>
<tr>
<td><strong>Implantation rate</strong></td>
<td>-0.012</td>
</tr>
<tr>
<td>Pregnancy chance</td>
<td>Exp(B): 0.051</td>
</tr>
</tbody>
</table>
RESULTS

Association between sperm count and ICSI outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sperm Count</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
<td>CI</td>
<td>p</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>0.075</td>
<td>0.020</td>
<td>0.035 – 0.115</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>High-quality embryos rate on D3</td>
<td>2.296</td>
<td>7.074</td>
<td>-11.587 – 16.179</td>
<td>0.746</td>
</tr>
<tr>
<td>Normal embryo development rate on D3</td>
<td>-0.884</td>
<td>0.568</td>
<td>-1.999 - 0.232</td>
<td>0.120</td>
</tr>
<tr>
<td>Blastocyst development rate</td>
<td>2.155</td>
<td>0.884</td>
<td>0.420 – 3.891</td>
<td>0.015</td>
</tr>
<tr>
<td>High-quality blastocysts rate</td>
<td>-36.970</td>
<td>27.177</td>
<td>-90.666 - 16.727</td>
<td>0.176</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>0.025</td>
<td>0.003</td>
<td>0.020 – 0.031</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pregnancy chance</td>
<td>Exp(B):</td>
<td>0.167</td>
<td>0.658 - 1.284</td>
<td>0.617</td>
</tr>
</tbody>
</table>
# RESULTS

**Association between progressive sperm motility and ICSI outcomes**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sperm Motility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>-0.003</td>
</tr>
<tr>
<td>High-quality embryos rate on D3</td>
<td>-1.573</td>
</tr>
<tr>
<td><strong>Normal embryo development rate on D3</strong></td>
<td><strong>0.017</strong></td>
</tr>
<tr>
<td>Blastocyst development rate</td>
<td>0.412</td>
</tr>
<tr>
<td>High-quality blastocysts rate</td>
<td>-5.955</td>
</tr>
<tr>
<td><strong>Implantation rate</strong></td>
<td><strong>0.183</strong></td>
</tr>
<tr>
<td>Pregnancy chance</td>
<td>Exp(B): 1.037</td>
</tr>
</tbody>
</table>
## RESULTS

**Association between total motile sperm count and ICSI outcomes**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total Motile Sperm Count</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
<td>CI</td>
<td>p</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>-0.007</td>
<td>0.030</td>
<td>-0.065 – 0.051</td>
<td>0.809</td>
</tr>
<tr>
<td>High-quality embryos rate on D3</td>
<td>2.841</td>
<td>2.297</td>
<td>-1.667 - 7.350</td>
<td>0.216</td>
</tr>
<tr>
<td>Normal embryo development rate on D3</td>
<td>-2.914</td>
<td>2.327</td>
<td>-7.480 - 1.652</td>
<td>0.211</td>
</tr>
<tr>
<td><strong>Blastocyst development rate</strong></td>
<td>1.057</td>
<td>0.508</td>
<td>0.060 – 2.054</td>
<td>0.038</td>
</tr>
<tr>
<td>High-quality blastocysts rate</td>
<td>9.779</td>
<td>6.442</td>
<td>-2.949 - 22.508</td>
<td>0.131</td>
</tr>
<tr>
<td><strong>Implantation rate</strong></td>
<td>0.008</td>
<td>0.003</td>
<td>0.002 – 0.014</td>
<td>0.009</td>
</tr>
<tr>
<td>Pregnancy chance</td>
<td>Exp(B): 0.957</td>
<td>0.062</td>
<td>0.845 - 1.083</td>
<td>0.475</td>
</tr>
</tbody>
</table>
DISCUSSION

Fertilization

Paternal age

Embryo development

Embryo implantation

Bias of the effect of maternal age on oocyte quality

Statistical tools: valuable in controlling maternal age

Oocyte donation cycles
DISCUSSION

Decreased IVF outcomes:
(Frattarelli et al. 2008; Luna et al. 2009)

No effect of paternal age on IVF outcomes
(Whitcomb et al. 2011; Begueria et al. 2014; Ghuman et al. 2016)

Oocyte donation cycles

Egg sharing donation population

VS

Young fertile oocyte donors
This creates an interesting situation

Oocytes from the same cohort can be compared

The impact of paternal age on the functionality of oocytes derived from infertile-couples can be analysed

This is different from most other published studies in which data comes from oocyte donor populations
Embryo development and implantation competence

Revisiting the impact of ejaculatory abstinence on semen quality and intracytoplasmic sperm injection outcomes

Keywords: Faculatory abstinence, ICSI, semen quality, sperm DNA fragmentation

Received: 13-Jul-2018
Revised: 6-Oct-2018
Accepted: 7-Nov-2018

Fertility Medical Group, Sao Paulo, Brazil, and Sapiens Institute, Sao Paulo, Brazil

fertilization, blastocyst formation, implantation, and pregnancy
Influence of ejaculatory abstinence on seminal total antioxidant capacity and sperm membrane lipid peroxidation
DISCUSSION

Sperm from infertile men undergo DNA damage, leading to impaired embryo development. The success rate (SDF) of ICSI outcomes is crucial with an SDF > 45% for a 45% pregnancy failure rate. 

Antonouli et al. 2019; Al Omrani et al. 2018; Evgeni et al. 2015

(Guerin et al. 2005)
DISCUSSION

Silber et al. 2003; Magli et al. 2009; Coates et al. 2015

severe male factor

aneuploid embryos

decreased implantation in man with poor semen quality

(Silber et al. 2003; Magli et al. 2009; Coates et al. 2015)
CONCLUSION

Increasing paternal age and EA, and poor semen parameters negatively impact ICSI outcomes, from fertilization to pregnancy.

Therefore further tracking of the impact of paternal characteristics on ICSI outcomes should be encouraged.

Despite paternal age is uncontrollable, and there are not so many things that can be done concerning semen quality, shortening of EA interval could be used as a strategy to optimize ICSI outcomes.
Few studies focused on the influence of male factors on IVF outcomes.

Conflicting results
Confound variables
Fertilization
Embryo development
Implantation

Seminal parameters
Paternal age
Ejaculatory abstinence length

ICSI outcomes