Microfluidic Sperm Selection Enhances ICSI Outcomes by Selecting Spermatozoa with the Highest Chromatin Integrity

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Abstract

Background

Sperm preparation methods aim at providing specimens for insemination with the highest progressive motility independent of phenotypic and genomic integrity. Both single-strand (ss) and double-strand (ds) DNA nicks and breaks inhibit the ability of the male genome to support embryonic development. While different mechanisms are in place to prevent this phenomenon, they may be hindered by a defective epididymal function or a suboptimal or aged oocyte.

Methods

From October 2016 to January 2019, consenting men (n=32) known to have higher DNA fragmentation in their ejaculate and prior ART failure had their ejaculates simultaneously processed by density gradient centrifugation (DGC) and MFSS. TUNEL was carried out on the raw specimens and on the differently selected aliquots. SCF was measured by terminal deoxynucleotidyltransferase dUTP nick-end labeling (TUNEL) on at least 500 spermatozoa under a fluorescent microscope utilizing a threshold of ≥15%. ICSI was performed in the standard fashion. In men (N=13) treated by ICSI with their female partners, clinical outcomes were recorded. Semen parameters, chromatin integrity, embryo implantation, and pregnancy characteristics were compared.

Conclusions

According to our study, SCF appears to be linked to the kinetic characteristics of the sperm cell. MFSS yielded the highest portion of progressive motility with the highest DNA integrity. This novel microfluidic system may serve to identify spermatozoa with the highest functional and genomic integrity.

Results

A total of 32 men with an average age of 41±9 years had the following average semen parameters: concentration of 48.1±37 x10^6/mL, motility of 31.5±14.6, and 2.4±1% morphology. After DGC and MFSS, the sperm concentration was 33.8±25 and 11.6±12 x10^6/mL, with 59.4±33% and 97.6±9% motility, respectively (P<0.0001). The morphology of the raw sperm sample improved from 2.4±1% to 4.0±1% after MFSS, while it remained at 2.6±1% after DGC (Table 1).

Table 1: Comparison of semen parameters between density gradient method and microfluidics

<table>
<thead>
<tr>
<th>Selection</th>
<th>N=32 Raw</th>
<th>Density Gradient</th>
<th>Microfluidics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male age (M±SD)</td>
<td>41.9</td>
<td>41±9</td>
<td>41±9</td>
</tr>
<tr>
<td>Concentration (x10^6/mL)</td>
<td>48.1±37</td>
<td>33.8±25</td>
<td>11.6±12</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>31.5±14.6</td>
<td>59.4±33</td>
<td>97.6±9</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>2.4±1</td>
<td>2.6±1</td>
<td>4.0±1</td>
</tr>
</tbody>
</table>

The average SCF decreased from 24% in raw samples to 15% following DGC and became 1.7% after MFSS processing (P<0.0001) (Figure 1). Couples (n=13) who underwent ICSI had an SCF in their raw sample of 30.3%, which reached 22% after DGC selection and was only 1.5% after MFSS (P < 0.0001). These couples (female age, 36.5±3 years; male age, 42±9 years) These couples female age, 36.5±3 years underwent 28 cycles with DGS sperm selection, achieving a fertilization rate of 67%.

DNA Strand Breakage

Figure 1. Comparison of DNA fragmentation between raw sperm and semen processed by DGC and MFSS

ICSI Outcome

Figure 2. Pregnancy outcome according to the sperm selection method

67% 41% 34% 31% 6.6% 8.6% 14.3%