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Summary

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REVIEW

High-magnification selection of spermatozoa prior to oocyte injection: confirmed and potential indications

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Florence Boitrelle, MD is working as an embryologist at Poissy General Hospital's assisted reproduction unit since 2009. She is currently working on her PhD thesis on the links between sperm morphology, nuclear quality, acrosome quality, genetics and epigenetics at the University of Versailles Saint-Quentin-en-Yvelines.

Abstract Intracytoplasmic morphologically selected sperm injection (IMSI) involves the use of differential interference contrast microscopy at high magnification (at least ×6300) to improve the observation of live human spermatozoa (particularly by showing sperm head vacuoles that are not necessarily seen at lower magnifications) prior to intracytoplasmic sperm injection (ICSI) into the oocyte. However, a decade after IMSI's introduction, the technique's indications and ability to increase pregnancy and/or birth rates (relative to conventional ICSI) are subject to debate. In an attempt to clarify this debate, this work performed a systematic literature review according to the PRISMA guidelines. The PubMed database was searched from 2001 onwards with the terms 'IMSI', 'MSOME' and 'high-magnification, sperm'. Out of 168 search results, 22 relevant studies reporting IMSI outcomes in terms of blastocyst, pregnancy, delivery and/or birth rates were selected and reviewed. The studies' methodologies and results are described and discussed herein. In view of the scarcity of head-to-head IMSI versus ICSI studies, the only confirmed indication for IMSI is recurrent implantation failure following ICSI. All other potential indications of IMSI require further investigation.

KEYWORDS: human spermatozoa, IMSI, MSOME, outcome, pregnancy rate, vacuole

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Comparison between intracytoplasmic sperm injection and intracytoplasmic morphologically selected sperm injection in oligo-astheno-teratozoospermia patients

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Abstract

Go to:

Objective

The aim of this study was to evaluate the efficiency of the intracytoplasmic morphologically selected sperm injection (IMSI) technique compared with conventional ICSI and previous ICSI attempts in oligo-astheno-teratozoospermia (OAT) patients.

Methods

The sperms were selected under high magnification (6,600×) and used to induce fertilization in previous ICSI patients by IMSI. These results were compared with previous conventional ICSI cycles in patients with OAT infertility.

Results

These results demonstrated no significant difference in the fertilization rate between IMSI and previous ICSI cycles (67.7% vs. 65.0%). However, the pregnancy and implantation rates with IMSI were significantly higher than those of the ICSI cycles (33.3% vs. 12.5% and 14.6% vs. 5.4%, respectively; $p<0.05$). The miscarriage rate among pregnant patients (18.2% vs. 37.5%) showed no statistically significant difference between groups.

Conclusion

Compared to conventional ICSI, this study found that IMSI increased the IVF-ET success rates in patients with OAT.

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ARTICLE

Low birth defects by deselecting abnormal spermatozoa before ICSI

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Abstract Consistent evidence from meta-analysis has linked assisted conception by IVF, and particularly intracytoplasmic sperm injection (ICSI), with an increased risk of major birth defects. To compare the risk of major malformations of children born after standard ICSI and after intracytoplasmic injection of morphologically selected spermatozoa (IMSI), a prospective population-based study was conducted from 2005 to 2010. ICSI and IMSI were performed in only one assisted reproduction unit according to its classification of spermatozoa and using fresh semen. Medical data and follow up during 2 years of 1028 infants were collected. Major malformations were identified and classified by an external independent physician. The two groups were similar concerning the parents' age, treatment, number of oocytes recovered, days of transfer, gestational age and birthweight. However, major malformations were significantly lower with IMSI (6/450, 1.33%) versus ICSI (22/578, 3.80%; adjusted odds ratio 0.35, 95% confidence interval 0.14–0.87, $P = 0.014$), mainly affecting boys (adjusted odds ratio 2.84, 95% confidence interval 1.24–6.53, $P = 0.009$). In conclusion, the significantly decreased risk of major birth defects associated with IMSI remained decreased after multivariate adjustment and highlights the beneficial effect of sperm selection before ICSI.

Eur J Obstet Gynecol Reprod Biol. 2013 Dec;171(2):286-90. doi: 10.1016/j.ejogrb.2013.09.006. Epub 2013 Sep 12.

Intracytoplasmic morphologically selected sperm injection is beneficial in cases of advanced maternal age: a prospective randomized study.

Setti AS[1], Figueira RC, Braga DP, Aoki T, Iaconelli A Jr, Borges E Jr.

Author information

Abstract

OBJECTIVE: To evaluate advanced maternal age as a rationale for performing intracytoplasmic morphologically selected sperm injection (IMSI).

STUDY DESIGN: This study included couples undergoing intracytoplasmic sperm injection (ICSI) as a result of advanced maternal age (≥37 years old). Sample size calculations were based on the assumption that a 15% difference in implantation rate would mean a clinically significant difference. To achieve this difference, 33 cycles would be needed in each treatment arm (with a significance level of 5% and power of 85%). Couples were randomly allocated to one of two sperm selection procedures (ICSI, n=33; or IMSI, n=33). Sperm selection in the ICSI group was analyzed under a magnification of 400×. Sperm selection in the IMSI group was analyzed under high magnification of 6600×. The groups were compared with regard to the outcome of the cycles.

RESULTS: IMSI cycles showed significantly higher implantation (4/33, 12.1% vs. 18/47, 38.3%, p=0.026) and pregnancy (4/29, 13.8 vs. 18/30, 60.0% p<0.001) rates. The IMSI procedure positively influenced the blastocyst formation rate (RC: 15.00, R2: 49.9%, p=0.001) and implantation rate (RC: 24.04, R2: 9.6, p=0.027), and was determinant to the increased odds of pregnancy (OR: 9.0, CI: 2.17-37.38, p=0.001).

CONCLUSION: It seems that the injection of a morphologically normal spermatozoon overcomes the low oocyte quality in older women, resulting in improved embryo quality and in a 9-fold increase in the clinical pregnancy rate in couples with advanced maternal age.

KEYWORDS: ICSI; IMSI; Oocyte quality; Sperm morphology

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REVIEW

Twelve years of MSOME and IMSI: a review

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Abstract A promising method for observing spermatozoa, motile sperm organelle morphology examination (MSOME) enables the evaluation of the nuclear morphology of motile spermatozoa in real time at high magnification and has allowed the introduction of a modified microinjection procedure, intracytoplasmic morphologically selected sperm injection (IMSI). Since its development, several studies have intensively investigated the efficacy of MSOME and IMSI. The objective of the present study is to review the current literature on the MSOME and IMSI techniques.

KEYWORDS: ICSI, IMSI, MSOME, sperm morphology

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Regular (ICSI) versus ultra-high magnification (IMSI) sperm selection for assisted reproduction.

Teixeira DM[1], Barbosa MA, Ferriani RA, Navarro PA, Raine-Fenning N, Nastri CO, Martins WP.

Author information

Abstract

BACKGROUND: Subfertility is a condition found in up to 15% of couples of reproductive age. Gamete micromanipulation, such as intracytoplasmic sperm injection (ICSI), is very useful for treating couples with compromised sperm parameters. Recently a new method of sperm selection named 'motile sperm organelle morphology examination' (MSOME) has been described and the spermatozoa selected under high magnification (over 6000x) used for ICSI. This new technique, named intracytoplasmic morphologically selected sperm injection (IMSI), has a theoretical potential to improve reproductive outcomes among couples undergoing assisted reproduction techniques (ART).

OBJECTIVES: To compare the effectiveness and safety of IMSI and ICSI in couples undergoing ART.

SEARCH METHODS: We searched for randomised controlled trials (RCT) in electronic databases (Cochrane Menstrual Disorders and Subfertility Group Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS), trials registers (ClinicalTrials.gov, Current Controlled Trials, World Health Organization International Clinical Trials Registry Platform), conference abstracts (ISI Web of knowledge), and grey literature (OpenGrey); in addition, we handsearched the reference lists of included studies and similar reviews. We performed the last electronic search on 8 May 2013.

SELECTION CRITERIA: We considered only truly randomised controlled trials comparing ICSI and IMSI to be eligible; we did not include quasi or pseudo-randomised trials. We included studies that permitted the inclusion of the same participant more than once (cross-over or 'per cycle' trials) only if data regarding the first treatment of each participant were available.

DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, data extraction, and assessment of the risk of bias and we solved disagreements by consulting a third review author. We corresponded with study investigators in order to resolve any queries, as required.

MAIN RESULTS: The search retrieved 294 records; from those, nine parallel design studies were included, comprising 2014 couples (IMSI = 1002; ICSI = 1012). Live birth was evaluated by only one trial and there was no significant evidence of a difference between IMSI and ICSI (risk ratio (RR) 1.14, 95% confidence interval (CI) 0.79 to 1.64, 1 RCT, 168 women, I(2) = not applicable, low-quality evidence). IMSI was associated with a significant improvement in clinical pregnancy rate (RR 1.29, 95% CI 1.07 to 1.56, 9 RCTs, 2014 women, I(2) = 57%, very-low-quality evidence). We downgraded the quality of this evidence because of imprecision, inconsistency, and strong indication of publication bias. We found no significant difference in miscarriage rate between IMSI and ICSI (RR 0.82, 95% CI 0.59 to 1.14, 6 RCTs, 552 clinical pregnancies, I(2) = 17%, very-low-quality evidence). None of the included studies reported congenital abnormalities.

AUTHORS' CONCLUSIONS: Results from RCTs do not support the clinical use of IMSI. There is no evidence of effect on live birth or miscarriage and the evidence that IMSI improves clinical pregnancy is of very low quality. There is no indication that IMSI increases congenital abnormalities. Further trials are necessary to improve the evidence quality before recommending IMSI in clinical practice.

Asian Journal of Andrology

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Focus on intracytoplasmic morphologically selected sperm injection (IMSI): a mini-review

Giuseppe Lo Monte,[1] Fabien Murisier,[2] Isabella Piva,[1] Marc Germond,[2] and Roberto Marci[1]

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Abstract

Go to:

Intracytoplasmic sperm injection (ICSI) is the recommended treatment in many cases of male-factor infertility. Several studies have demonstrated a positive correlation between optimal sperm morphology and positive ICSI outcomes. In fact, spermatozoa with severe abnormalities of the head are well documented to be associated with low fertilisation, implantation and pregnancy rates. However, a spermatozoon which is classified as 'normal' by microscopic observation at low magnification could contain ultrastructural defects that impair both the fertilisation process and embryonic development. The intracytoplasmic morphologically selected sperm injection (IMSI) procedure changed the perception of how a spermatozoon suitable for injection should appear. Sperm selection is carried out at ×6000 magnification, allowing improved assessment of the sperm nucleus. Currently, standardized clinical indications for IMSI are lacking and the candidates are selected on the grounds of their medical history or of a careful analysis of the sperm suspension. Further prospective randomized studies are needed to confirm the advantages of IMSI in specific groups of patients. In addition to providing a brief overview of the IMSI procedure, this study aims to review the literature, which explains the theoretical basis and the clinical outcomes of this technique. Several reports show that IMSI is associated with improved implantation and clinical pregnancy rates as well as lower abortion rates when compared to ICSI. Although a possible correlation between the sperm's abnormal nucleus shape, increased DNA fragmentation and negative laboratory and clinical outcomes has been long investigated, the results are conflicting.

Keywords: assisted reproduction technologies, ICSI, IMSI, infertility

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ANDROLOGIA

Original Article

Quality of human spermatozoa: relationship between high-magnification sperm morphology and DNA integrity

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Keywords:
Apoptosis; DNA integrity; human; morphology; spermatozoa

Summary

The aim of this work is to establish the relationship between the morphology of Intracytoplasmic Morphologically Selected Sperm Injection (IMSI)-selected spermatozoa and their DNA integrity. The 45 ejaculates were randomly distributed into three treatment groups: normozoospermic, oligoasthenozoospermic and oligoasthenotheratozoospermic samples. The evaluation of DNA integrity was performed using the sperm chromatin dispersion test. It was established that DNA integrity of spermatozoa is strongly dependent on ejaculate quality ($P < 0.05$). The count of spermatozoa with nonfragmented DNA in normozoospermic samples was high and independent from IMSI-morphological classes (Class 1 versus Class 3, respectively) ($P > 0.1$). With decreased ejaculate quality, the percentage of spermatozoa with nonfragmented DNA decreased significantly ($P < 0.05$) independent from morphological class. Nevertheless, the rate of IMSI-selected spermatozoa with fragmented DNA within of Class 1 in normozoospermic (Group 1), in oligoasthenozoospermic (Group 2) and in oligoasthenotheratozoospermic (Group 3) samples was 21.1%, 31.8% and 54.1%, respectively. In conclusion, there is a direct relationship between morphological parameters of spermatozoa and their DNA integrity. However, the IMSI technique alone is not enough for the selection of spermatozoa with intact nuclei.

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human reproduction update

Motile sperm organelle morphology examination (MSOME) and sperm head vacuoles: state of the art in 2013

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TABLE OF CONTENTS

BACKGROUND: Approximately 10 years after the first publication introducing the motile sperm organelle morphology examination (MSOME), many questions remained about sperm vacuoles: frequency, size, localization, mode of occurrence, biological significance and impact on male fertility potential. Many studies have tried to characterize sperm vacuoles, to determine the sperm abnormalities possibly associated with vacuoles, to test the diagnostic value of MSOME for male infertility or to question the benefits of intracytoplasmic morphologically selected sperm injection (IMSI).

METHODS: We searched PubMed for articles in the English language published in 2001–2012 regarding human sperm head vacuoles, MSOME and IMSI.

RESULTS: A bibliographic analysis revealed consensus for the following findings: (i) sperm vacuoles appeared frequently, often multiple and preferentially anterior; (ii) sperm vacuoles and sperm chromatin immaturity have been associated, particularly in the case of large vacuoles; (iii) teratozoospermia was a preferred indication of MSOME and IMSI.

CONCLUSION: The high-magnification system appears to be a powerful method to improve our understanding of human spermatozoa. However, its clinical use remains unclear in the fields of male infertility diagnosis and assisted reproduction techniques (ARTs).

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Intracytoplasmic morphologically selected sperm injection outcomes: the role of sperm preparation techniques

Edson Borges, Jr.,✉ Amanda Souza Setti, Livia Vingris, Rita de Cassia Savio Figueira, Daniela Paes de Almeida Ferreira Braga, and Assumpto Iaconelli, Jr.

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Abstract

Go to:

Purpose

To compare the results of intracytoplasmic morphologically selected sperm injection (IMSI) between cycles in which the swim-up (SUP) or the density gradient centrifugation (DGC) techniques were used for sperm preparation.

Methods

We evaluated 70 IMSI cycles performed in women with age ≤ 37 years, undergoing IMSI as result of male factor. The couples were divided into two groups: DGC group ($n = 26$) and SUP group ($n = 44$). The groups were compared with regard to IMSI outcomes.

Results

There were no significant differences between SUP and DGC groups regarding the number of follicles, oocytes, mature oocytes, oocyte yield and mature oocyte rate. Fertilization rate and high-quality embryos rate on day 5 of development were similar between SUP and DGC groups. Implantation, pregnancy and miscarriage rates were not statistically different between SUP and DGC groups (28.8 vs 33.3 %, 46.2 vs 57.1 % and 8.3 vs 4.2 %, respectively).

Conclusions

Both the SUP and the DGC techniques recover improved sperm fractions and result in similar IMSI

J Assist Reprod Genet

ORIGINAL ARTICLES: ANDROLOGY

Is intracytoplasmic morphologically selected sperm injection effective in patients with infertility related to teratozoospermia or repeated implantation failure?

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Objective: To evaluate the potential benefit of intracytoplasmic morphologically selected sperm injection (IMSI) in patients selected for either severe teratozoospermia or repeated implantation failure after conventional intracytoplasmic sperm injection (ICSI).
Design: Prospective nonrandomized observational study.
Setting: University hospital assisted reproduction unit.
Patient(s): Four hundred seventy-eight patients were enrolled to evaluate ICSI and IMSI results for two indications. The first group (T) was composed of patients with severe teratozoospermia (<10% normal spermatozoa in fresh ejaculated and selected semen, according to David classification) and no or one previous ICSI failure. In the second group (IF), patients with at least two previous failed ICSI attempts were enrolled in absence of severe male factor (>10% normal spermatozoa in fresh ejaculated semen and >20% in selected sperm).
Intervention(s): ICSI/IMSI, biologic, and clinical data collection.
Main Outcome Measure(s): Live-birth rate (LBR).
Result(s): In group T, LBR was significantly higher when IMSI procedure was used compared with ICSI (38% [50/132] vs. 20% [25/126]). However, LBR observed in group IF was not significantly different between IMSI and ICSI procedures (21% [19/90] vs. 22% [28/130]).
Conclusion(s): IMSI procedure is a valuable option for patients with severe teratozoospermia at their first or second attempts, but it does not improve pregnancy rate in patients with repeated ICSI failures in the absence of severe male factor. (Fertil Steril® 2013;100:62–8. ©2013 by American Society for Reproductive Medicine.)
Key Words: ICSI, IMSI, high-magnification spermatozoa selection, live birth rate

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Sperm vacuoles negatively affect outcomes in intracytoplasmic morphologically selected sperm injection in terms of pregnancy, implantation, and live-birth rates

Ermanno Greco, M.D.,[a] Filomena Scarselli, M.Sc.,[a] Gemma Fabozzi, M.Sc.,[a] Alessandro Colasante, Ph.D.,[a] Daniela Zavaglia, M.D.,[a] Erminia Alviggi, Ph.D.,[a] Katarzyna Litwicka, M.D.,[a] Maria Teresa Varricchio, M.D.,[a] Maria Giulia Minasi, M.Sc.,[a] and Jan Tesarik, M.D.[b]

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Objective: To retrospectively evaluate whether sperm vacuoles influence clinical results, with a particular focus on live-birth rates, in 101 intracytoplasmic morphologically selected sperm injection (IMSI) cycles.
Design: Retrospective, observational study.
Setting: Medical center.
Patient(s): A total of 101 couples with at least two failed intracytoplasmic sperm injection (ICSI) attempts and impaired sperm morphology.
Intervention(s): Patients divided into two groups according to sperm morphology and vacuolization pattern: group A comprising patients with good quality spermatozoa (type I and/or type II spermatozoa) (n = 63 patients); group B comprising patients with low quality spermatozoa (type III and/or IV spermatozoa) (n = 38 patients).
Main Outcome Measure(s): Fertilization rate, embryo quality, pregnancy, implantation, and live-birth rates.
Result(s): No statistically significant differences were observed between group A and B with regard to "early" assisted reproduction outcomes (fertilization rate and embryo quality). However, the "late" outcomes (pregnancy, implantation, and live-birth rates) were statistically significantly higher in group A.
Conclusion(s): These results confirm a correlation between sperm vacuoles and a negative IMSI 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, IMSI, live-birth rate, morphologically selected sperm injection, vacuoles

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ARTICLE

Developmental dynamics of IMSI-derived embryos: a time-lapse prospective study

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Katja Knez obtained her biotechnology degree in 2009 from the University of Ljubljana in the field of male infertility. She is now a PhD student of Assistant Professor Dr Irma Virant-Klun in the IVF Lab, Department of Obstetrics and Gynaecology, University Medical Centre Ljubljana, Slovenia. Her current research area is clinical embryology, especially the basics and clinical application of intracytoplasmic morphologically selected sperm injection and time-lapse imaging of embryo development.

Abstract Because sperm vacuoles were marked as zones without chromatin in the sperm nucleus, which may reflect underlying chromosomal or DNA defects, this study considered whether they influence the morphology and dynamics of early developmental events in preimplantation embryos. Oocytes were injected with spermatozoa of four classes, according to the number and size of vacuoles at ×6000 magnification, and derived embryos were observed under time-lapse microscopy. For each embryo, the times of pronuclei appearance and disappearance and the first, second and third divisions were determined and related to its respective class of injected spermatozoa and its developmental stage. Embryos arising from normal class-I spermatozoa (without vacuoles) reached the 4-cell stage significantly earlier than embryos developed from class-IV spermatozoa (with large vacuoles and other abnormalities) ($P = 0.012$). Blastocysts from class-I spermatozoa required the shortest mean time for all developmental events in comparison with blastocysts from spermatozoa of other classes (with vacuoles). Blastocysts also showed significantly earlier first division than arrested embryos in embryos arising from class-I spermatozoa ($P = 0.033$). An insight into the developmental dynamics of embryo development according to morphology and head vacuoles of injected spermatozoa in morphologically selected sperm-derived embryos was observed for the first time.