Surgical Sperm Retrieval and Increased Sperm DNA Fragmentation

1. Testicular versus ejaculated sperm should be used for intracytoplasmic sperm injection (ICSI) in cases of infertility associated with sperm DNA fragmentation | Opinion: Yes.

   Author(s): Esteves, Sandro C
   Source: International braz j urol : official journal of the Brazilian Society of Urology; 2018; vol. 44 (no. 4); p. 667-675
   Publication Date: 2018
   Publication Type(s): Editorial
   PubMedID: 30020584
   Available at International braz j urol - from PubMed Central
   Database: Medline

2. Testicular versus ejaculated sperm should be used for intracytoplasmic sperm injection (ICSI) in cases of infertility associated with sperm DNA fragmentation | Opinion: No.

   Author(s): Sigman, Mark
   Source: International braz j urol : official journal of the Brazilian Society of Urology; 2018; vol. 44 (no. 4); p. 676-679
   Publication Date: 2018
   Publication Type(s): Editorial
   PubMedID: 30020585
   Available at International braz j urol - from PubMed Central
   Database: Medline
3. Use of testicular sperm for intracytoplasmic sperm injection in men with high sperm DNA fragmentation: A SWOT analysis

**Author(s):** Esteves S.; Roque M.; Garrido N.

**Source:** Asian Journal of Andrology; 2018; vol. 20 (no. 1); p. 1-8

**Publication Date:** 2018

**Publication Type(s):** Review

Available at Asian Journal of Andrology - from Europe PubMed Central - Open Access

**Abstract:** Spermatozoa retrieved from the testis of men with high levels of sperm DNA fragmentation (SDF) in the neat semen tend to have better DNA quality. Given the negative impact of SDF on the outcomes of Assisted Reproductive Technology (ART), an increased interest has emerged about the use of testicular sperm for intracytoplasmic sperm injection (Testi-ICSI). In this article, we used a SWOT (strengths, weaknesses, opportunities, and threats) analysis to summarize the advantages and drawbacks of this intervention. The rationale of Testi-ICSI is bypass posttesticular DNA fragmentation caused by oxidative stress during sperm transit through the epididymis. Hence, oocyte fertilization by genomically intact testicular spermatozoa may be optimized, thus increasing the chances of creating a normal embryonic genome and the likelihood of achieving a live birth, as recently demonstrated in men with high SDF. However, there is still limited evidence as regards the clinical efficacy of Testi-ICSI, thus creating opportunities for further confirmatory clinical research as well as investigation of Testi-ICSI in clinical scenarios other than high SDF. Furthermore, Testi-ICSI can be compared to other laboratory preparation methods for deselecting sperm with damaged DNA. At present, the available literature supports the use of testicular sperm when performing ICSI in infertile couples whose male partners have posttesticular SDF. Due to inherent risks of sperm retrieval, Testi-ICSI should be offered when less invasive treatments for alleviating DNA damage have failed. A call for continuous monitoring is nonetheless required concerning the health of generated offspring and the potential complications of sperm retrieval. Copyright © 2017 The Author(s).

**Database:** EMBASE


**Author(s):** Soygur, Bikem; Celik, Soner; Celik-Ozenci, Ciler; Sati, Leyla

**Source:** Journal of assisted reproduction and genetics; Mar 2018; vol. 35 (no. 3); p. 491-501

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29150736

Available at Journal of Assisted Reproduction and Genetics - from SpringerLink

**Abstract:** The purpose of this study is to investigate whether erythrocyte-sperm separation medium (ESSM) has effects on human sperm motility, morphology, viability, membrane maturity, acrosome integrity, and nuclear attributes before and after cryopreservation. Samples from normozoospermic (n = 36) and oligozoospermic (n = 9) patients were analyzed. Samples from the same patient were divided into three aliquots: group 1 and group 2 were resuspended in sperm washing media and ESSM, respectively. Group 3 was resuspended in ESSM with blood sample to mimic the extensive number of erythrocytes in the testicular sperm extraction (TESE) material. All groups were evaluated for sperm concentration, motility, Kruger/Tygerberg strict morphology, viability by eosin-nigrosin staining, membrane maturity by hyaluronic acid-binding assay (HBA), acrosomal integrity by Pisum sativum lectin staining, chromatin maturity by aniline blue
staining, and DNA integrity by TUNEL assay before and after cryopreservation.

RESULTS
No significant difference was determined between ESSM-treated and ESSM-untreated sperm samples for the sperm parameters tested (p > 0.05). After cryopreservation, total sperm motility and viability decreased regardless of ESSM used. The percentages of sperm with Tygerberg normal morphology, intact acrosome, and HA-bound sperm were found to be lower in oligozoospermic samples before cryopreservation in each group. However, no statistically significant differences were found between oligozoospermic and normozoospermic samples when all groups were compared. Thus, ESSM treatment did not cause a significant change on sperm motility, normal morphology, viability, HA-binding capacity, chromatin maturity, and DNA fragmentation.

CONCLUSION
ESSM can enhance the efficiency of sperm retrieval protocol and can also decrease the time required to collect spermatozoa while not affecting sperm morphogenetic properties.

Database: Medline

5. ICSI outcome in patients with high DNA fragmentation: Testicular versus ejaculated spermatozoa.

Author(s): Arafa, M; AlMalki, A; AlBadr, M; Burjaq, H; Majzoub, A; AlSaid, S; Elbardisi, H

Source: Andrologia; Feb 2018; vol. 50 (no. 1)

Publication Date: Feb 2018

Publication Type(s): Journal Article

PubMedID: 28497461

Available at Andrologia - from Wiley Online Library Science, Technology and Medicine Collection 2017

Abstract: Sperm DNA fragmentation (SDF) has emerged as an important biomarker in the assessment of male fertility potential with contradictory results regarding its effect on ICSI. The aim of this study was to evaluate intracytoplasmic sperm injection (ICSI) outcomes in male patients with high SDF using testicular versus ejaculated spermatozoa. This is a prospective study on 36 men with high-SDF levels who had a previous ICSI cycle from their ejaculates. A subsequent ICSI cycle was performed using spermatozoa retrieved through testicular sperm aspiration. Results of the prior ejaculate ICSI were compared with those of the TESA-ICSI. The mean (SD) SDF level was 56.36% (15.3%). Overall, there was no difference in the fertilization rate and embryo grading using ejaculate and testicular spermatozoa (46.4% vs. 47.8%, 50.2% vs. 53.4% respectively). However, clinical pregnancy was significantly higher in TESA group compared to ejaculated group (38.89% [14 of 36] vs. 13.8% [five of 36]). Moreover, 17 live births were documented in TESA group, and only three live births were documented in ejaculate group (p < .0001). We concluded that the use of testicular spermatozoa for ICSI significantly increases clinical pregnancy rate as well as live-birth rate in patients with high SDF.

Database: Medline
6. Testicular sperm for ICSI in men with high DFI Can it be made a Recommendation?

**Author(s):** Arun Karthik P.; Vasan S.S.; Karthik K.N.; Madhumitha M.

**Source:** Indian Journal of Urology; Jan 2018; vol. 34 (no. 5); p. 19

**Publication Date:** Jan 2018

**Publication Type(s):** Conference Abstract

Available at [Indian Journal of Urology](https://www.indianjournalurology.com) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:** Despite clear breakthrough in the field of ART we are still unable to pull up the pregnancy rates beyond 35-40%. What is it that we are missing? Sperm DNA fragmentation has emerged as an important biomarker for assessing male fertility potential. Many studies have postulated that one of the mechanisms involved in sperm DNA fragmentation is ROS-induced DNA damage during comigration of mature sperm with ROS-producing immature sperm through the seminiferous tubules and epididymis. This can be bypassed by testicular sperm aspiration. Materials and methods Retrospective, observational, cohort study conducted at our Fertility center from June 2015 till December 2016. Group A : EjaculateICSI n=37 Group B : TesticularICSI n=39 Inclusion criteria Infertility duration >1 year Couples undergoing IVFICSI No abnormality noted in the medical history, physical examination and endocrine profile Persistent high SDF levels (>30%) in two semen specimens, SDF performed using the SCSA flowcytometry analysis No evidence of subclinical genital infections and/or leukocytospermia Women with average to good quality oocytes on retrieval Exclusion criteria Severe male factor infertility (severe oligoasthenoteratozoospermia, <5 million/mL; and azoospermia) Women with history of poor response to ovarian stimulation, including those fitting the Bologna criteria for expected poor responders Patients in whom oocyte or sperm donation was used Any uterine pathology like fibroid uterus, Adenomyosis which could impact implantation Results The two groups were homogeneous regarding to age, endocrine profile, infertility duration and the proportion of females with an associated infertility problem No difference in no of oocytes retrieved in the two groups. Fertilization rate was lower in the Testicular ICSI group (64.6%) compared to EjaculateICSI group (73.6%), however not statistically significant. Pregnancy rates were higher in the TesticularICSI group 48.7% vs Ejaculate ICSI 38.7% Miscarriage rates were remarkably low in TesticularICSI group than the Ejaculate ICSI group(15.7%vs 35.7%) It was noted that the pregnancy rates in men with DFI in the range of 3040 was not different. (53.3% in Ejaculate and 46.1% in Testicular group) A significantly higher pregnancy rate was observed in the Testicular group when the ranges of DFI was higher than 40 Interestingly it was observed that in patients with DFI more than 50 pregnancy almost never occurred with ejaculate sperms and better pregnancy rates were observed with Testicular sperms. Conclusion DNA fragmentation index is an important biomarker for assessing male fertility potential and should be made a part of routine evaluation. Testicular sperm is associated with improved ICSI outcomes in men with high DFI. DFI cut off for labelling a patient with high DFI needs reconsideration.

**Database:** EMBASE
7. Reproductive outcomes of testicular versus ejaculated sperm for intracytoplasmic sperm injection among men with high levels of DNA fragmentation in semen: systematic review and meta-analysis.

**Author(s):** Esteves, Sandro C; Roque, Matheus; Bradley, Cara K; Garrido, Nicolás

**Source:** Fertility and Sterility; Sep 2017; vol. 108 (no. 3); p. 456

**Publication Date:** Sep 2017

**Publication Type(s):** Meta-analysis Comparative Study Journal Article Review

**PubMedID:** 28865546

**Abstract:**

OBJECTIVE: To compare sperm DNA fragmentation (SDF) levels between testicular and ejaculated sperm and to evaluate outcomes of intracytoplasmic sperm injection (ICSI) with the use of testicular (Testi-ICSI) versus ejaculated (Ejac-ICSI) sperm in nonazoospermic men with high SDF.

DESIGN: Systematic review and meta-analysis.

SETTING: Not applicable.

PATIENT(S): Normo- and oligozoospermic men with high levels of SDF in semen subjected to Testi-ICSI or Ejac-ICSI.

INTERVENTION(S): Summary mean difference (MD) and odds ratio (OR) were calculated with the use of an inverse variance model and fixed- or random-effects models, respectively.

MAIN OUTCOME MEASURE(S): Primary outcomes were SDF levels, clinical pregnancy rates (CPRs), and live birth rates (LBRs). Secondary outcomes were fertilization and miscarriage rates.

RESULT(S): Five studies involving 143 patients provided paired SDF rates for testicular and ejaculated sperm, revealing lower SDF in testicular sperm (MD -24.58%). Four studies involving 507 cycles and 3,840 oocytes reported clinical outcomes of Testi-ICSI and Ejac-ICSI. Fertilization rates were not different between sperm sources, but a trend to lower rates was observed with Testi-ICSI. CPRs were higher for Testi-ICSI than for Ejac-ICSI, as were LBRs, whereas miscarriage rates were reduced with Testi-ICSI. CONCLUSION(S): Testicular sperm have lower levels of SDF than ejaculated sperm, with Testi-ICSI for high post-testicular SDF men improving reproductive outcomes compared with Ejac-ICSI. Infertile couples may benefit from Testi-ICSI if male partners have confirmed high SDF in the ejaculate.

Database: Medline

8. Sperm source influences the extent of DNA fragmentation and shapes reproductive outcome

**Author(s):** Parrella A.; O’Neill C.; Chow S.; Rosenwaks Z.; Palermo G.D.; Goldstein M.

**Source:** Fertility and Sterility; Sep 2017; vol. 108 (no. 3)

**Publication Date:** Sep 2017

**Publication Type(s):** Conference Abstract

**Abstract:**

OBJECTIVE: During the later stages of spermatogenesis, DNA breakage is physiologically required to allow tight chromatin compaction. While most spermatozoa undergo DNA repair, reactive oxygen species (ROS) are the main cause for DNA injury. We question whether sperm chromatin integrity differs among spermatozoa isolated from different sections of the male genital tract and how it may affect reproductive outcome. DESIGN: Over 42 months, men with high SCF in their ejaculates (n=77) underwent surgical sampling, often bilateral, from vas deferens, epididymis, and testis. SCF was assessed by TUNEL, and clinical outcome was recorded for each sperm source for men undergoing ICSI treatment. MATERIALS AND METHODS: Ejaculates processed in the standard fashion were assessed for SCF by TUNEL. Surgical samples were minced and prepared for SCF evaluation and were cryopreserved for later use with ICSI. DNA fragmentation was measured by TUNEL on specimens isolated from all sites. TUNEL was executed by utilizing a commercial kit (In Situ Cell Death Detection Kit, Roche). At least 500 spermatozoa were counted per site under fluorescent microscopy with an adopted threshold of 15%. RESULTS: Of the original 77 patients, 54 were treated by ART with an average SCF of 23.7+/- 11.7% (11.8-42.3) in their ejaculate. In 10 men aspiration of the vas deferens resulted in 19.9+/- 6.4% SCF (range 35-5.8) while in 41 men epididymal sampling
yielded 16.0 +/- 7.6% SCF (range 38.4-5.3) and in 77 the SCF on testicular spermatozoa was 11.5+/-5.7% (range 31.2-1.5). The SCF progressively decreased as TUNEL was measured proximally from the ejaculate toward the vas deferens (P=0.02), the epididymis (P=0.005), and testis (P<0.001). A fertilization of 68.3% (287/420), 79.4% (124/156) and 60.3% (251/416) was achieved by ICSI using ejaculated, epididymal, and testicular spermatozoa, respectively. While the clinical pregnancy rate in ejaculated spermatozoa was only 21.2%, ART outcome with ICSI utilizing these surgical sources yielded a clinical pregnancy of 35.8%. Based on these preliminary findings a subgroup of patients (n=28), with SCF of 30.5 +/- 17.4 bypassed the prerequisite cycle with ejaculated spermatozoa and opted to undergo TESE with ICSI. The clinical pregnancy rate achieved was 35.0% per cycle that translated to 50% per couple treated. CONCLUSIONS: DNA integrity assessment on the spermatozoa isolated at different levels of the male genital tract evidenced that oxidative stressors progressively alter DNA integrity toward the ejaculate. Couples unable to achieve a pregnancy using ejaculated spermatozoa with compromised DNA may benefit from undergoing testicular retrieval for diagnostic and therapeutic purposes.

**Database:** EMBASE

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9. Testicular versus ejaculated sperm in men without azoospermia: A systematic review and meta-analysis

**Author(s):** Awaga H.; Kolibianakis E.; Bosdou J.; Goulis D.; Grimbizis G.; Tarlatzis B.

**Source:** Human Reproduction; Jul 2017; vol. 32

**Publication Date:** Jul 2017

**Publication Type(s):** Conference Abstract

**Abstract:** Study question: In couples without azoospermia, is the probability of pregnancy higher when testicular as compared to ejaculated sperm is used for ICSI? Summary answer: In couples without azoospermia, the probability of pregnancy is higher when testicular as compared to ejaculated sperm is used for ICSI. What is known already: Currently, testicular sperm extraction (TESE) is performed in patients with azoospermia, while in the presence of even a few spermatozoa in the ejaculate, this invasive procedure can be avoided. Some couples, however, repeatedly fail to achieve pregnancy despite successful fertilization. In these cases, the use of surgically retrieved spermatozoa has been proposed. In fact, this concept has also been evaluated in couples with normal semen analysis but high DNA fragmentation index. However, it is not yet clear whether the probability of pregnancy is higher when testicular as compared to ejaculated sperm is used for ICSI in couples without azoospermia. Study design, size, duration: A systematic review and meta-analysis was performed aiming to identify trials evaluating whether the probability of pregnancy is higher when testicular as compared to ejaculated sperm is used for ICSI in couples without azoospermia. For this purpose, a relevant literature search was carried out until December 2016. Primary outcome measure was achievement of pregnancy, expressed as clinical pregnancy or live birth. Secondary outcome measures were fertilization rate, number of 2-pronuclei (2pn) oocytes and miscarriage rate. Participants/materials, setting, methods: One prospective and five retrospective comparative studies offering data to answer the research question were identified including a total of 754 couples who performed 839 ICSI cycles. Meta-analysis of weighted data using random and fixed effects model was performed. Results are reported as relative risk (RR) or weighted mean differences (WMD) with 95% confidence intervals (CI). Main results and the role of chance: No significant differences were observed between the two groups compared regarding male age, male FSH, testicular volume and DFI, female FSH, antral follicle count, endometrial thickness, number of retrieved oocytes, number of MII oocytes, the number of embryos transferred and the proportion of patients reaching ET. However, female age was significantly higher in the testicular group compared with the ejaculate group (WMD +1.56, 95%CI: +0.66 to +2.46), while female BMI was significantly
lower in the testicular group as compared to the ejaculate group (WMD: -1.23, 95%CI: -2.07 to -0.39). A significantly higher probability of live birth rate both per started cycle (RR: 1.72, 95%CI 1.28-2.31) and per embryo transfer (ET) (RR: 1.66, 95%CI 1.25-2.22) was present in the TESE as compared to the ejaculate group. Similarly, a significantly higher probability of clinical pregnancy, both per started cycle (RR: 1.51, 95%CI 1.20-1.91) and per ET (RR: 1.54, 95%CI 1.23-1.93) as well as a lower probability of miscarriage (RR: 0.38, 95%CI 0.21-0.71) were present in the TESE as compared to the ejaculate group. No significant difference was present in the fertilization rate in the TESE as compared to the ejaculate group (WMD: 6.84, 95%CI -17.53 to +3.86). Limitations, reasons for caution: The results of the current meta-analysis are based on a limited number of non-randomized studies that do not allow for additional subgroup analyses. In addition, differences have been observed in baseline characteristics between the populations compared that could affect the primary outcome measure assessed. Wider implications of the findings: The findings of the current metaanalysis, if confirmed, might lead to important changes in the management of patients without azoospermia undergoing ICSI due to male factor. However, it is imperative prior to routinely adopting TESE for ICSI in these patients, to confirm the current results by appropriate randomized controlled trials.

Database: EMBASE

10. Testicular versus ejaculated spermatozoa in ICSI cycles of normozoospermic men with high sperm DNA fragmentation and previous ART failures.

Author(s): Pabuccu, E G; Caglar, G S; Tangal, S; Haliloglu, A H; Pabuccu, R

Source: Andrologia; Mar 2017; vol. 49 (no. 2)

Publication Date: Mar 2017

Publication Type(s): Comparative Study Journal Article

PubMedID: 27108915

Available at Andrologia - from Wiley Online Library Science, Technology and Medicine Collection 2017

Abstract: As a part of male assessment, conventional sperm parameters including morphologic features have been dedicated as major factors influencing fertilisation and pregnancy rates in assisted reproductive technology (ART). Genomic integrity of spermatozoa has also been found to influence fertility prognosis, and hence, sperm DNA fragmentation index (DFI) has been adopted by many centres to document this entity. Despite several suggested approaches, there is lack of universal consensus on optimising fertility outcomes in males with high sperm DFI. In this context, the results from cycles using testicular spermatozoa (TESA) obtained by aspiration were compared with those of ejaculated spermatozoa (EJ) in normozoospermic subjects with high sperm DFI and previous ART failures. Clinical (41.9% versus 20%) and ongoing pregnancy rates (38.7% versus 15%) were significantly better and miscarriages were lower in TESA group when compared to EJ group. Sperm DFI should be a part of male partner’s evaluation following unsuccessful ART attempts. When high DFI is detected (>30%), ICSI using testicular spermatozoa obtained by TESA seems an effective option particularly for those with repeated ART failures in terms of clinical, ongoing pregnancies and miscarriages even though conventional sperm parameters are within normal range.

Database: Medline
11. Testicular sperm aspiration (TESA) for infertile couples with severe or complete asthenozoospermia

**Author(s):** Al-Malki A.H.; Alrabeeah K.; Zini A.; Mondou E.; Brochu-Lafontaine V.; Phillips S.

**Source:** Andrology; Mar 2017; vol. 5 (no. 2); p. 226-231

**Publication Date:** Mar 2017

**Publication Type(s):** Article

**PubMedID:** 28187532

Available at [Andrology](https://onlinelibrary.wiley.com/journal/10.1111) - from Wiley Online Library Science, Technology and Medicine Collection 2017

**Abstract:** The aim of the study was to evaluate reproductive outcomes in a cohort of infertile couples with severe and complete asthenozoospermia undergoing TESA (testicular sperm aspiration) with ICSI. We conducted a retrospective study of 28 couples with complete or severe asthenozoospermia who underwent TESA between January 2010 and December 2015. We compared TESA-ICSI outcomes of these couples to ejaculate ICSI outcomes of 40 couples with severe asthenozoospermia treated during the same time period at our institution. Couples with female factor infertility and/or female aged >= 39 were excluded. Sperm retrieval rates and ICSI outcomes [(MII oocytes, fertilization rate, good embryo rate (transferred and frozen), couples with embryo transfer (per cycle started), clinical pregnancy (per embryo transfer)] were recorded. Patients were grouped based on whether they had ejaculated (Ej-group) or testicular (TESA-group) spermatozoa used. Testicular sperm patients were further classified based on whether they had complete asthenozoospermia (0% total motility) (Tc-group) or severe asthenozoospermia (=1% progressive motility) (Ts-group). Mean (+/-SD) male and female ages were 36 +/- 6 and 32 +/- 4, respectively. Sperm recovery by testicular sperm aspiration (TESA) was successful in 100% (28/28) of the men. The overall clinical pregnancy rate (CPR) per cycle started was 34% (23/68) with a mean of 1.1 +/- 0.4 embryos transferred per transfer. Fertilization rates were significantly lower in TESA-group compared to Ej-group (52% vs. 67%, respectively; p = 0.001), while male age was significantly higher in TESA-group compared to Ej-group (34 +/- 6 vs. 37 +/- 6, respectively; p = 0.03). Moreover, female age was significantly higher in Tc-group compared to Ts-group (30 +/- 4 vs. 33 +/- 3, respectively; p = 0.0285). However, there were no significant difference in clinical pregnancy rate per embryo transfer in the Tc-group, Ts-group, and Ej-group (50% vs. 45% vs. 57%, respectively; p = 0.8219). The data suggest that testicular sperm-ICSI is no better than ejaculated sperm-ICSI in couples with severe or complete asthenozoospermia. Randomized, controlled trials comparing ejaculated vs. testicular spermatozoa are needed to assess the true benefit of TESA-ICSI in these couples. Copyright © 2017 American Society of Andrology and European Academy of Andrology.

**Database:** EMBASE
15. Intervention improves assisted conception intracytoplasmic sperm injection outcomes for patients with high levels of sperm DNA fragmentation: a retrospective analysis.

Author(s): Bradley, C K; McArthur, S J; Gee, A J; Weiss, K A; Schmidt, U; Toogood, L

Source: Andrology; Sep 2016; vol. 4 (no. 5); p. 903-910

Publication Date: Sep 2016

Publication Type(s): Journal Article

PubMedID: 27231097

Available at Andrology - from Wiley Online Library Science, Technology and Medicine Collection 2017

Abstract: Sperm DNA fragmentation (SDF) is used in assisted reproductive technology (ART) programs as an indicator for sperm quality, although there is still a lack of consensus as to its clinical utility. In this retrospective study, we examined intracytoplasmic sperm injection (ICSI) outcomes of 1924 infertile patients who underwent SDF analysis using the sperm chromatin integrity test. ART patients were classified as having low [DNA fragmentation index (DFI) <29%] or high SDF (DFI ≥29%) and by whether or not an intervention [physiological intracytoplasmic sperm injection (PICSI), intracytoplasmic morphologically selected sperm injection (IMSI), testicular sperm extraction (TESE)/testicular sperm aspiration (TESA), frequent ejaculation] was performed. High SDF patients who did not have an intervention had a lower fertilization rate and poorer clinical outcomes from blastocyst transfers as compared with low SDF patients; the fertilization rate was 66.0% vs. 70.2% (p = 0.042), single embryo transfer (SET) fetal heart pregnancy rate was 28.5% vs. 45.2% (p = 0.042), and SET live birth rate was 24.9% vs. 40.6% (p = 0.060), respectively. Furthermore, high SDF patients who had an intervention had significantly improved blastocyst transfer outcomes, similar to those of low SDF patients; the SET live birth rate for high SDF intervention patients was 43.8% as compared with 24.2% for high SDF patients who did not have an intervention, PICSI patients had 38.3% (p = 0.151), IMSI patients had 28.7% (p = 0.680), and TESE/TESA patients had 49.8% (p = 0.020). Our data suggest that SDF results indicate ICSI outcomes and that patients who have high SDF benefit from an intervention.

Database: Medline

13. DNA fragmentation in relation to sperm source and reproductive outcome

Author(s): Paniza T.; Cozzubbo T.; Cheung S.; Parrella A.; Rosenwaks Z.; Palermo G.D.; Goldstein M.

Source: Fertility and Sterility; Sep 2016; vol. 106

Publication Date: Sep 2016

Publication Type(s): Conference Abstract

Abstract: OBJECTIVE: During the later stages of spermiogenesis DNA breakage is physiologically required to allow tight chromatin compaction. While most spermatozoa undergo DNA repair, reactive oxygen species (ROS) are the main cause for DNA injury. We question whether sperm chromatin integrity differs among spermatozoa isolated at different sections of the male genital tract and how it may affect reproductive outcome. DESIGN: Over 30 months, men with high SCF in their ejaculates (n=74) underwent surgical sampling, often bilateral, from vas deferens, epididymis, and testis. SCF was assessed by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and clinical outcome was recorded for each sperm source for men undergoing ICSI treatment. MATERIALS AND METHODS: Ejaculates processed in the standard fashion were assessed for SCF by TUNEL. Surgical samples were minced and prepared for SCF evaluation and were...
cryopreserved for later use with ICSI. DNA fragmentation was measured by TUNEL on specimens isolated from all sites. TUNEL was executed by utilizing a commercial kit (In Situ Cell Death Detection Kit, Roche). At least 500 spermatozoa were counted per site under fluorescent microscopy with an adopted threshold of 15%. RESULTS: Of the original 74 patients, 33 were treated by ART with an average SCF of 27.4 +/- 17% (range 26.0-96.0) in their ejaculate. In 10 men aspiration of the vas deferens resulted in 18.6 +/- 8% SCF (range 5.8-30.0) while in 40 men epididymal sampling yielded 17.1 +/- 8% SCF (range 5.3-34.8) and in 74 the SCF on testicular spermatozoa was 11.7 +/- 6% (range 2.0-27.0). The SCF progressively decreased as TUNEL was measured proximally from the ejaculate toward the vas deferens (P=0.03), the epididymis (P=0.001), and testis (P=0.001). A fertilization of 63.4% (281/443), 65.2% (58/89) and 59.9% (217/362) was achieved by ICSI using ejaculated, epididymal, and testicular spermatozoa, respectively. ART outcome with ICSI utilizing these surgical sources yielded a clinical pregnancy of 26.4%, while with the ejaculated counterpart only 14.6%. Based on these preliminary findings a subgroup of patients (n=19), with SCF of 40.1 +/- 18 bypassed the prerequisite cycle with ejaculated spermatozoa and opted to undergo TESE with ICSI. The clinical pregnancy rate achieved was 29.0% per cycle that translated to 55.6% per couple treated.

CONCLUSIONS: DNA integrity assessment on the spermatozoa isolated at different levels of the male genital tract evidenced that oxidative stressors progressively compromise DNA integrity toward the ejaculate, this may be obviated by utilizing testicular spermatozoa. Couples unable to achieve a pregnancy using ejaculated spermatozoa with compromised DNA may benefit from undergoing testicular retrieval for diagnostic and therapeutic purposes.

Database: EMBASE
underwent 1363 cycles and included women with an average age of 37.7 +/- 4 years and men with a mean age of 39.8 +/- 5 years. The overall average sperm concentration was 50.0 +/- 29 million with a motility of 49.9 +/- 14% and morphology of 3.1 +/- 2%. Based on the control, we expect an intrauterine insemination (IUI) clinical pregnancy rate of 17.9%, but the study cohort evidenced a clinical pregnancy rate of just 3.4%. The patients from this cohort presented a TUNEL of 26.1 +/- 18% and SCSA DFI of 39.5 +/- 26%. Men with normal SCF were subsequently treated by in vitro insemination and reported a pregnancy rate of 22.1%. Once we controlled for an eventual confounding female factor (female age <=35 years), a remarkably higher pregnancy rate of 36.8% (P < 0.001) was reached. On the other hand, couples with abnormal DFI were treated exclusively by ICSI also yielding a higher pregnancy rate at 21.7%, and 28.9% with females 35 years old (P < 0.001). For those patients that failed ICSI with ejaculated spermatozoa, we offered a testicular sampling. In 38 couples that consented, the SCF of testicular spermatozoa was 12.3 +/- 6%, remarkably lower than 39% SCF in the ejaculate, and a pregnancy rate of 26.7% (P < 0.001). Limitations, reasons for caution: Patients need to be informed of risks regarding surgery, anesthesia, and the possibility that even with TESE a pregnancy may not occur. Thus, engaging counseling should be conducted since these men have spermatozoa in their ejaculate. These data are still preliminary and a clinical consensus has not been reached. Wider implications of the findings: IVF is successful in men with intact sperm chromatin. When sperm SCF is compromised in the ejaculate, ICSI is the most suitable insemination method. In men with high DNA fragmentation in their ejaculate and pursuant pregnancy failure, surgical sampling yields spermatozoa with lower SCF and higher changes of pregnancy.

Database: EMBASE

15. Meaning of DNA fragmentation in relation to the sperm source and ART outcome

Author(s): Paniza T.; Cozzubbo T.; Chow S.; Cheung S.; Neri Q.V.; Rosenwaks Z.; Palermo G.D.; Goldstein M.

Source: Human Reproduction; Jul 2016; vol. 31

Publication Date: Jul 2016

Publication Type(s): Conference Abstract

Available at Human Reproduction - from Oxford Journals - Medicine

Abstract: Study question: We question whether sperm chromatin integrity differs among spermatozoa isolated from different sections of the male genital tract and how it affects reproductive outcome. Summary answer: Progression through the male genital tract increases chances for oxidative aggression and consequent sperm chromatin fragmentation (SCF), this may be obviated by utilizing testicular spermatozoa. What is known already: During the later stages of spermiogenesis DNA breakage is physiologically induced to allow tight chromatin compaction. While most spermatozoa undergo DNA repair, additional reactive oxygen species (ROS) are the main cause for DNA injury. The buffering capacity of seminal antioxidants is the only agent protecting the DNA integrity of spermatozoa in the ejaculate. Therefore, retrieving spermatozoa from the epididymis or testis may bypass such an insult on the chromatin. Study design, size, duration: Over 27 months, men with extremely high SCF in their ejaculates (n = 64) underwent surgical sampling, often bilateral, from vas deferens, epididymis, and testis. SCF was assessed by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and clinical outcome was recorded for each sperm source for men undergoing ICSI. Participants/materials, setting, methods: Ejaculates processed in standard fashion were assessed for SCF by TUNEL. Surgical samples were minced and smeared for SCF evaluation and were cryopreserved for later use with ICSI. DNA fragmentation was measured by TUNEL on specimens isolated from all sites. TUNEL was assessed utilizing a commercial kit (In Situ Cell Death Detection Kit, Roche). At least 500 spermatozoa were evaluated per site under fluorescent microscopy with an adopted threshold of 15%. Main results and the role of chance: Of the original
64 patients, 51 were treated by ART with an average SCF of 31.0 +/- 19% (range 26.0-96.0). In 9 men aspiration of the vas deferens resulted in 16.7 +/- 8% SCF (range 5.8-30.0) while in 32 men epididymal sampling yielded 17.3 +/- 8% SCF (range 7.0-34.8) and in 64 the SCF on testicular spermatozoa was 12.3 +/- 6% (range 2.0-27.0). The SCF progressively decreased as TUNEL was performed proximally from the ejaculate toward the vas deferens (P = 0.05), the epididymis (P = 0.01), and testis (P = 0.01). ART outcome with ICSI utilizing these surgical sources yielded a clinical pregnancy of 26.7%, while with the ejaculated counterpart only 14.6%. Based on these preliminary findings a subgroup of patients (n = 19), with SCF of 40.1 +/- 18 bypassed the prerequisite cycle with ejaculated spermatozoa. By opting to directly undergo TESE with ICSI a clinical pregnancy rate of 29.0% per cycle was achieved that translated to 55.6% per couple treated. Limitations, reasons for caution: Patients need to be informed of risks regarding surgery, anesthesia, and be aware that even with surgical spermatozoa a pregnancy may not occur. Thus, engaging counseling should be conducted since many of these men have spermatozoa in their ejaculate. These data are still preliminary and require an evidence-based consensus. Wider implications of the findings: DNA integrity assessment on the spermatozoa isolated at different levels of the male genital tract evidenced that oxidative stressors progressively compromise DNA integrity toward the ejaculate. Couples unable to achieve a pregnancy using ejaculated spermatozoa with compromised DNA may benefit from undergoing testicular retrieval for diagnostic and therapeutic purposes.

Database: EMBASE

16. Improved fertility outcomes following testicular sperm aspiration in men with elevated sperm DNA fragmentation indices

Author(s): Patel N.; Mike; Hsieh T.C.
Source: Journal of Urology; Apr 2016; vol. 195 (no. 4)
Publication Date: Apr 2016
Publication Type(s): Conference Abstract

Abstract: INTRODUCTION AND OBJECTIVES: An elevated sperm deoxyribonucleic acid fragmentation index (DFI) correlates with poor semen parameters and inferior pregnancy outcomes. Prior studies have demonstrated lower DFI in testicular sperm versus ejaculated sperm. However, the utilization of sperm DFI for the treatment of infertility is unclear. We sought to demonstrate fertility outcomes in patients with high DFI using testicular sperm aspiration (TESA) for intracytoplasmic sperm injection (ICSI). METHODS: Men with elevated DFI (>24%) were recruited from a single male fertility center. Sperm DFI was measured using sperm chromatin structure assay from a single lab. Previous assisted reproductive technology outcomes as well as demographic data of the partner were recorded. TESA was performed with an 18G needle under local anesthesia and in-cycle ICSI was implemented. Fertility outcomes were analyzed. RESULTS: We identified 44 men with DFI >24% from ejaculate sperm. 28 of these patients previously failed ICSI or had history of miscarriage. 17 couples (38.6%) achieved clinical pregnancy following TESA and in-cycle ICSI. Of the couples that previously failed ICSI or had history of miscarriage, 42.9% achieved clinical pregnancy. An increase in the mean fertility rate was observed with current TESA ICSI cycle compared to previous ejaculate sperm cycles (55.4% vs 36.9%, p=0.009). An improvement in the mean number of high quality embryos with the current TESA ICSI cycle compared to previous ejaculate sperm cycles was also observed (7 vs 4, p=0.01). A lower sperm DFI was observed in the pregnant group (35.2% vs 37.2%, p=0.54).
CONCLUSIONS: In cycle TESA is associated with improved fertility outcome in men with elevated sperm DFI. Patients whom failed ICSI or with history of miscarriages, sperm DFI testing is indicated and testicular sperm retrieval should be offered in appropriate patients. Future studies are needed to validate our findings. (Table Presented).

Database: EMBASE
17. Comparison of reproductive outcome in oligozoospermic men with high sperm DNA fragmentation undergoing intracytoplasmic sperm injection with ejaculated and testicular sperm.

Author(s): Esteves, Sandro C; Sánchez-Martín, Fernando; Sánchez-Martín, Pascual; Schneider, Danielle T; Gosálvez, Jaime

Source: Fertility and sterility; Dec 2015; vol. 104 (no. 6); p. 1398-1405

Publication Date: Dec 2015

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Multicenter Study Journal Article Observational Study

PubMedID: 26428305

Abstract: OBJECTIVE To investigate the effectiveness of intracytoplasmic sperm injection (ICSI) using testicular sperm as a strategy to overcome infertility in men with high sperm DNA fragmentation (SDF). DESIGN Prospective, observational, cohort study. SETTING Private IVF centers. PATIENT(S) A total of 147 couples undergoing IVF-ICSI and day 3 fresh ETs whose male partner has oligozoospermia and high SDF. INTERVENTION(S) Sperm injections were carried out with ejaculated sperm (EJA-ICSI) or testicular sperm (TESTI-ICSI) retrieved by either testicular sperm extraction (TESE) or testicular sperm aspiration (TESA). SDF levels were reassessed on the day of oocyte retrieval in both ejaculated and testicular specimens. MAIN OUTCOME MEASURE(S) Percentage of testicular and ejaculated spermatozoa containing fragmented DNA (%DFI) and clinical pregnancy, miscarriage, and live-birth rates. RESULT(S) The %DFI in testicular sperm was 8.3%, compared with 40.7% in ejaculated sperm. For the TESTI-ICSI group versus the EJA-ICSI group, respectively, the clinical pregnancy rate was 51.9% and 40.2%, the miscarriage rate was 10.0% and 34.3%, and the live-birth rate was 46.7% and 26.4%. CONCLUSION(S) ICSI outcomes were significantly better in the group of men who had testicular sperm used for ICSI compared with those with ejaculated sperm. SDF was significantly lower in testicular specimens compared with ejaculated counterparts. Our results suggest that TESTI-ICSI is an effective option to overcome infertility when applied to selected men with oligozoospermia and high ejaculated SDF levels.

Database: Medline


Author(s): Mehta, Akanksha; Bolyakov, Alexander; Schlegel, Peter N; Paduch, Darius A

Source: Fertility and sterility; Dec 2015; vol. 104 (no. 6); p. 1382-1387

Publication Date: Dec 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26363389

Abstract: OBJECTIVE To evaluate assisted reproductive technology (ART) outcomes using testicular sperm in oligospermic men who previously failed to achieve paternity using TUNEL-positive ejaculated sperm. DESIGN Retrospective cohort study. SETTING Academic medical center. PATIENT(S) Twenty-four oligospermic men who failed one or more ART cycles using ejaculated sperm with TUNEL-positive proportion >7%, and subsequently underwent microsurgical testicular sperm extraction (TESE). INTERVENTION(S) TESE followed by intracytoplasmic sperm injection (ICSI). MAIN OUTCOME MEASURE(S) TUNEL-positive level in ejaculated and testicular sperm; clinical pregnancy. RESULT(S) The mean TUNEL-positive level was 24.5% for ejaculated sperm, and 4.6% for testicular sperm. Clinical pregnancy was achieved in the first ART cycle with testicular sperm in 12 (50%) out of 24 couples. There was no statistically significant difference in maternal and paternal age, maternal gravity and parity, number of previous ART attempts, concentration or motility of retrieved sperm, number of oocytes retrieved, fertilization rate, or number of embryos transferred...
between couples who did and did not achieve pregnancy. No miscarriages occurred. All 12 pregnancies resulted in the delivery of healthy children.

CONCLUSION(S)
The percentage of TUNEL-positive cells is lower in testicular sperm for oligospermic men who have abnormal ejaculated sperm DNA fragmentation. The use of testicular sperm for ICSI was associated with a 50% pregnancy and live-birth rate for couples who had previously failed one or more IVF-ICSI cycles with ejaculated sperm. No other clinical predictors of successful pregnancies after the use of surgically retrieved sperm could be identified. In men with elevated TUNEL-positive ejaculated sperm and failed ART, TESE may be considered.

Database: Medline

19. Testicular sperm extraction in the management of patients with RIF and severe male factor infertility: A case series

Author(s): Meaney C.; Cutting R.

Source: Human Fertility; 2014; vol. 17 (no. 4)

Publication Date: 2014

Publication Type(s): Conference Abstract

Abstract: Introduction Recurrent Implantation Failure (RIF) is the failure to achieve a clinical pregnancy following the transfer of multiple good quality embryos. This can be extremely distressing for couples and can, even following multiple investigations, remain unexplained in the majority of cases. One causative factor in RIF couples with severe male factor may be a high rate of sperm DNA damage leading to genetic abnormalities and aneuploidy in embryos with subsequent implantation failure. Although the exact mechanism of sperm DNA damage remains unclear, studies have shown that ejaculated-derived sperm can contain up to 3-fold higher levels of sperm DNA damage than that of TESE-derived sperm. Methods Seven couples selected for elective testicular sperm extraction (eTESE) following RIF were reviewed. Results Following eTESE-ICSI treatment 4 out of 7 couples achieved implantation (38.46%) and a clinical pregnancy (57.14%). There were no significant difference however in fertilisation rates (40-41 31.98 vs 62.37 20.03, p=0.15) or utilisation rates (68.33 32.49, p=0.44) when the last ejaculate-ICSI cycle was compared to the eTESE-ICSI cycle respectively. Conclusion This case series review suggests that eTESE should continue to be offered to this select group of patients on a case-to-case basis. In addition we aim to extend the use of eTESE and consider its application in the treatment of other patient groups such as those with poor embryo quality or development, and those with underlying conditions pre-disposing them to high rates of sperm DNA fragmentation.

Database: EMBASE
20. Comparison of DNA fragmentation levels in testicular sperm extraction (TESE) samples from patient with obstructive and non-obstructive azoospermia and effect on outcome from intracytoplasmic sperm injection (ICSI)

Author(s): Allahveisi A.

Source: International Journal of Urology; Dec 2014; vol. 21

Publication Date: Dec 2014

Publication Type(s): Conference Abstract

Abstract: Introduction: Azoospermia is defined as an absence of sperm in the semen ejaculate, and it concluded obstructive and nonobstructive. Obstructive azoospermia is the result of an obstruction in the male reproductive tract. Non-obstructive azoospermia is the result of severely impaired sperm production, which exhibits either in obstructive and nonobstructive forms. Therefore, This study was conducted to determine sperm DNA fragmentation in patient with obstructive and non-obstructive azoospermia has an effect on fertilization and clinical pregnancy rates after intracytoplasmic sperm injection (ICSI). Methods: motile and immotile sperm are obtained in azoospermic patient with obstructive and non-obstructive. Azoospermic patients undergoing intracytoplasmic sperm injection cycles. DNA fragmentation was determined using Sperm Chromatin Dispersion (SCD) kit. Results: Testicular sperm retrieval was performed on the day of oocyte retrieval in each patient groups. The groups were comparable in terms of the ages of male and female patients, ovarian response to stimulation, as well as the number of oocytes injected. The number of cycles with non-obstructive azoospermia and obstructive azoospermia was evenly distributed in each group. Fertilization rates were 72%, 51.8.7%, clinical pregnancy rate 28.3 and 20.5% for patient with obstructive and non-obstructive azoospermia, respectively. Conclusion: Our results showed that sperm DNA fragmentation in patient with non-obstructive azoospermia different from patient with obstructive azoospermia. Moreover, it has an effect on fertilization and clinical pregnancy rate after intracytoplasmic sperm injection (ICSI).

Database: EMBASE


Author(s): Qiu, Yi; Wang, Lei-Guang; Zhang, Li-Hong; Zhang, Ai-Dong; Wang, Zhong-Ye

Source: Journal of andrology; 2012; vol. 33 (no. 5); p. 1036-1046

Publication Date: 2012

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 22441760

Available at Journal of andrology - from Wiley Online Library Science, Technology and Medicine Collection 2017

Abstract: The aim of this study was to explore sperm chromosomal aneuploidy and DNA integrity in infertile patients with spinal cord injury (SCI). Semen samples were collected from 12 infertile men with SCI by percutaneous vasal sperm aspiration (PVSA) and from 14 male SCI patients by penile vibratory stimulation (PVS). These semen samples as well as samples from 16 donors were analyzed using the hypo-osmotic swelling (HOS) test, the sperm chromatin dispersion test, terminal deoxynucleotidyl transferase-mediated terminal uridine nick-end labeling assay, and multicolor fluorescence in situ hybridization with probes specific for the chromosomes 13, 18, 21, X, and Y. There were significant differences in the percentages of motile sperm, normal morphologic sperm, normal HOS/eosin staining, and sperm DNA fragmentation between the infertile men with SCI and the control group (P < .05 and P < .01). The sperm forward motility was significantly greater in the
PVSA group than in the PVS group \( (P < .01) \). The number of round cells per milliliter of semen obtained from the 14 SCI patients by PVS was between 1 million and 12 million. The rate of sperm DNA fragmentation, as identified by the sperm chromatid dispersion test, was higher in the PVS group than in the PVSA group \( (P < .05) \). The aneuploidy rates for the SCI patients were 1.5- to 1.6-fold higher for chromosomes 13, 18, and 21, and were 2.3- to 2.4-fold higher for chromosomes X and Y than for patients in the control group \( (P < .001) \). These results suggest that for men with SCI, the semen quality is poorer, the prevalence of abnormal HOS/eosin staining is greater, and sperm DNA fragmentation and sperm chromosomal aneuploidies are seen at a higher rate compared with healthy, fertile, and normospermic men.

**Database:** Medline

### 22. DNA fragmentation in sperm collected in testis and different epididymal regions from the same azoospermic patients

**Author(s):** Hammoud I.; Izard V.; Albert M.; Bergere M.; Bailly M.; Boitrelle F.; Vialard F.; Wainer R.; Selva J.

**Source:** Human Reproduction; 2011; vol. 26

**Publication Date:** 2011

**Publication Type(s):** Conference Abstract

**Abstract:** Introduction: Even if testicular or epididymal sperm retrieval is positive for most patients with obstructive azoospermia (OA), pregnancy and implantation rates remain quite low. In OA, whatever is the etiology of obstruction, sperm DNA damages could be increased by trapping and stagnation, or by a slowdown transit of sperm or by an increased pressure upper the obstruction and bedeleterious for the embryo. The aim of this study was (i) to evaluate DNA fragmentation of surgically retrieved spermatozoa and in different etiologies of OA, (ii) to improve the ICSI results by choosing the less DNA fragmented sample for injection.

**Material and Methods:** Twenty patients with OA and both epididymal and testicular sperm retrieval (MESA and TESE) were included. In this study, OA was defined by bioclinical and ultrasonographic evaluation, normal testis histology, normal serum FSH and inhibit B levels, decreased biochemical epididymal markers; 4 patients had congenital bilateral absence of vas deferens - CBAVD, 8 post-genital tract infection and 8 unknown etiology. Testicular spermatozoa were extracted by mechanical dilaceration of the testis fragments and epididymal sperm cells were aspirated in a syringe. We compared the rates of DNA fragmentation of spermatozoa collected in the testis, the epididymis caput and the epididymis corpus. Just after preparation of straws for ICSI, remaining spermatozoa were spread on slides and kept at -20degreeC. DNA fragmentation was evaluated by a TUNEL assay performed with the Cell Death Detection Kit (Roche Diagnostics, Milan, Italy) as described by the manufacturer (normal value is below 13% with this technique in our laboratory). Results: Among the 20 patients, 14 patients exhibited sperm both in testis biopsy, caput and corpus epididymis punctures and 6 patients had no sperm in corpus of epididymis. A total of 45726 spermatozoa were analyzed. They were retrieved intestis \( (n = 7888) \), in the epididymis caput \( (n = 18958) \) or in the epididymis corpus \( (n = 18880) \). Testicular spermatozoa were less often DNA fragmented than those retrieved in the epididymis caput \( (6.84 +/- 0.77% vs 14.63 +/- 1.90%; p < 0.005) \) and than the spermatozoa retrieved in the epididymis corpus \( (6.84 +/- 0.77% vs 32.92 +/- 3.12%; p < 0.0001) \). Furthermore spermatozoa retrieved in epididymis caput were less often DNA fragmented than those retrieved in the corpus \( (14.63 +/- 1.90% vs 32.92 +/- 3.12%; p < 0.0001) \). These results were found in each of the 3 groups of patients, CBAVD, infectious and unknown etiology of obstructive azoospermia. Conclusion: Testicular sperm DNA fragmentation rate was lower than epididymal sperm DNA fragmentation rate and this whatever was the etiology of obstructive azoospermia. These results suggest that longer is the aging of spermatozoa after spermiation, higher is their risk to be DNA fragmented. Since epididymal sperm
DNA fragmentation rates were above the normal cut-off, these data suggest that the use of testicular sperm during ICSI attempts should be counselled for all patients with obstructive azoospermia.

**Database:** EMBASE

**23. Effects of semen storage and separation techniques on sperm DNA fragmentation.**

**Author(s):** Jackson, Robert E; Bormann, Charles L; Hassun, Pericles A; Rocha, André M; Motta, Eduardo L A; Serafini, Paulo C; Smith, Gary D

**Source:** Fertility and sterility; Dec 2010; vol. 94 (no. 7); p. 2626-2630

**Publication Date:** Dec 2010

**Publication Type(s):** Comparative Study Journal Article Evaluation Studies

**PubMedID:** 20542505

**Abstract:**

**OBJECTIVE:** To determine the effect of semen storage and separation techniques on sperm DNA fragmentation.

**DESIGN:** Controlled clinical study.

**SETTING:** An assisted reproductive technology laboratory.

**PATIENT(S):** Thirty normozoospermic semen samples obtained from patients undergoing infertility evaluation.

**INTERVENTION(S):**

- One aliquot from each sample was immediately prepared (control) for the sperm chromatin dispersion assay (SCD).
- Aliquots used to assess storage techniques were treated in the following ways: snap frozen by liquid nitrogen immersion, slow frozen with Tris-yolk buffer and glycerol, kept on ice for 24 hours or maintained at room temperature for 4 and 24 hours.
- Aliquots used to assess separation techniques were processed by the following methods: washed and centrifuged in media, swim-up from washed sperm pellet, density gradient separation, density gradient followed by swim-up. DNA integrity was then measured by SCD.

**MAIN OUTCOME MEASURE(S):** DNA fragmentation as measured by SCD.

**RESULT(S):**

- There was no significant difference in fragmentation among the snap frozen, slow frozen, and wet-ice groups. Compared to other storage methods short-term storage at room temperature did not impact DNA fragmentation yet 24 hours storage significantly increased fragmentation.
- Swim-up, density gradient and density gradient/swim-up had significantly reduced DNA fragmentation levels compared with washed semen.
- Postincubation, density gradient/swim-up showed the lowest fragmentation levels.

**CONCLUSION(S):** The effect of sperm processing methods on DNA fragmentation should be considered when selecting storage or separation techniques for clinical use.

**Database:** Medline
24. Use of testicular sperm/intracytoplasmic sperm injection yields high pregnancy rates in couples who failed multiple in vitro fertilization cycles owing to high levels of sperm DNA fragmentation

**Author(s):** Werthman P.; Boostanfar R.; Chang W.; Chung K.; Danzer H.; Koopersmith T.; Ringler G.; Shamonki M.; Surrey M.; Vermesh M.; Wilcox J.

**Source:** Fertility and Sterility; Mar 2010; vol. 93 (no. 5)

**Publication Date:** Mar 2010

**Publication Type(s):** Conference Abstract

**Abstract:** BACKGROUND: Sperm DNA damage (fragmentation) is a known cause of male factor infertility and has been shown to negatively impact pregnancy outcomes in couples undergoing IVF with intracytoplasmic sperm injection (ICSI). Previous studies have shown that sperm DNA damage may occur after the sperm have exited the testicle and that levels of DNA fragmentation are lower in testicular sperm than in ejaculated sperm. OBJECTIVE(S): To evaluate the results of IVF/ICSI using testicular sperm in couples who failed to achieve pregnancy on prior IVF cycles and who had high levels of sperm damage as a cause of their infertility. MATERIALS AND METHOD(S): We retrospectively reviewed the charts of 24 consecutive patients who underwent testicular sperm extraction for use with ICSI between January 1, 2008, and August 1, 2008. All patients had sperm present in the ejaculate that tested with a high DNA fragmentation index (DFI) as measured by sperm chromatin structure assay. All patients had failed to achieve pregnancy during prior IVF cycles using ejaculated sperm. In an effort to improve the chances of conception, couples elected to have sperm harvested directly from the testicle and used for IVF/ICSI. Ovarian hyperstimulation was performed by one of 10 different reproductive endocrinologists at five different assisted reproductive technology laboratories in the Los Angeles area. Testicular sperm extraction was performed by a single surgeon (PW) on the day of oocyte retrieval or 1 day prior. RESULT(S): All men had at least one abnormal semen parameter and a high DFI (>30%) ranging from 32% to 82%, with a mean of 51.6%. The etiology of sperm damage included varicocele, pyospermia, infection, partial obstruction, cryptorchidism, steroid abuse, and idiopathic. The average age of the female partner was 36.4 years, with a range of 32-46 years. Two couples used an egg donor, and the wives’ ages were excluded from the aforementioned calculation. All couples had undergone between one and seven prior ICSI attempts with a mean of three failed cycles. A pregnancy rate of 62.5% was achieved when testicular sperm were used. An 83% pregnancy rate was achieved when the DFI was over 65%. A 75% pregnancy rate was achieved in couples who underwent four or more prior failed IVF cycles. CONCLUSION(S): These data show that the use of testicular sperm/ICSI provides an efficient treatment option for couples who fail multiple IVF cycles because of high levels of sperm DNA fragmentation. Neither the degree of sperm DNA damage nor the number of prior failed IVF cycles appeared to affect the ability to achieve pregnancy when testicular sperm were used.

**Database:** EMBASE
25. Sperm DNA fragmentation levels in testicular sperm samples from azoospermic males as assessed by the sperm chromatin dispersion (SCD) test.

**Author(s):** Meseguer, Marcos; Santiso, Rebeca; Garrido, Nicolas; Gil-Salom, Manuel; Remohí, Jose; Fernandez, Jose Luis

**Source:** Fertility and sterility; Nov 2009; vol. 92 (no. 5); p. 1638-1645

**Publication Date:** Nov 2009

**Publication Type(s):** Research Support, Non-u.s. Gov't Journal Article Evaluation Studies

**PubMedID:** 19006791

**Abstract:**

OBJECTIVE To analyze sperm DNA fragmentation (SDF) in testicular sperm samples from patients with azoospermia either from spermatogenic failure or from duct obstruction. Several technologies can be applied in the evaluation of SDF, but given the ease and low costs, the sperm chromatin dispersion test (SCD) has emerged as a promising standard. DESIGN Prospective blind observational cohort study. SETTING University-affiliated private IVF setting. PATIENT(S) Azoospermic patients from couples undergoing intracytoplasmic sperm injection cycles. INTERVENTION(S) Testicular sperm extraction (TESE). MAIN OUTCOME MEASUREMENT(S) We determined testicular SDF, and a basic comparison between nonobstructive (n = 22) and obstructive azoospermia (n = 40) was performed. We also correlated SDF with embryo quality and pregnancy outcome. RESULT(S) SDF in the testicular sperm of patients with nonobstructive azoospermia was significantly higher, 46.92% (SEM = 4.47), than that of patients with obstructive azoospermia, 35.96% (SEM = 2.63). A moderate relationship between embryo morphology and testicular SDF was detected. Logistic regression analysis of the effect of testicular SDF on pregnancy outcome revealed no significant effect (odds ratio = 1.015). CONCLUSION(S) Ours is the first report of SDF analysis in testicular sperm by using SCD in azoospermia. This result suggests that spermatogenesis failure may result in a severe affectation of sperm DNA integrity. The degree of DNA fragmentation using the SCD test is not reflected in pregnancy chances, and the explanation could be that embryos have been selected.

**Database:** Medline
26. Interim analysis of a randomized controlled trial comparing ICSI outcomes using testicular vs. ejaculated sperm in men with persistently elevated sperm DNA fragmentation

**Author(s):** Wehbi E.; Moskovitsev S.; Spencer L.; Meriano J.; Cadesky J.; Hannan T.; Jarvi K.A.; Lo K.C.

**Source:** Journal of Urology; Apr 2009; vol. 181 (no. 4); p. 729-730

**Publication Date:** Apr 2009

**Publication Type(s):** Conference Abstract

**Abstract:** INTRODUCTION AND OBJECTIVE: Elevated sperm DNA fragmentation has been associated with poor natural pregnancy rates and linked to worsening of several parameters in assisted reproductive technologies (ART). Previous work has shown that testicular extracted sperm has a lower rate of DNA damage compared to ejaculated sperm from the same subject. It has been proposed that using testicular sperm in men with high sperm DNA damage and multiple ICSI failures may improve pregnancy outcomes (Greco et al 2005). Here we present our preliminary data from a prospective, randomized, controlled trial of men randomized to either testicular sperm extraction (TESE) or ejaculate sperm for ICSI. METHODS: Nineteen men with a persistently elevated sperm DNA Fragmentation Index (DFI) after completing a 3-month course of antioxidants have been enrolled in our study so far. The couples were then randomized to an ICSI cycle using fresh TESE or ejaculate sperm. The initial sperm DFIs were performed. On the day of ICSI, both ejaculated and testicular sperm were analysed using the TUNEL assay. Based on the previous reported ICSI outcomes (Greco et al, 2005), we powered our study to see a 35% difference in clinical pregnancy rates with 20 couples in each arm. We perform the interim analysis to assess potential risks and complications from the additional intervention (TESE) and evaluate the results of the ICSI cycles. RESULTS: Of the 19 couples enrolled, 15 completed the study. Three couples withdrew from the study and one couple had their cycle canceled due to poor ovulation stimulation. The TUNEL stained sperm DNA fragmentation rates were significantly lower in the testicular sperm group compared to the ejaculated sperm group (p<0.01). There were no reported complications from the TESEs performed. Chemical and clinical pregnancies were accomplished in 4/7 (57%) couples using testicular sperm and 2/8 (25%) using ejaculated sperm for ICSI. The difference has not reached statistical significance due to the low subject numbers in this interim study, as expected. CONCLUSIONS: Our interim analysis showed a trend towards increasing clinical pregnancy rates using testicular extracted sperm. This data is preliminary and it is premature to conclude that TESE should be the standard of care for couples with an elevated DFI undergoing ICSI. With no complications reported thus far, we will continue the RCT and expand our sample size to better power our study to show a difference between the groups, if one truly exists.

**Database:** EMBASE
27. Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for azoospermia.

Author(s): Van Peperstraten, A; Proctor, M L; Johnson, N P; Philipson, G

Source: The Cochrane database of systematic reviews; Apr 2008 (no. 2); p. CD002807

Publication Date: Apr 2008

Publication Type(s): Meta-analysis Journal Article Review

PubMedID: 18425884

Available at Cochrane Database of Systematic Reviews: Reviews - from Cochrane Collaboration (Wiley)

Abstract: BACKGROUND Azoospermia, the absence of sperm in ejaculated semen, is the most severe form of male-factor infertility and is present in approximately 5% of all investigated infertile couples. The advent of intra-cytoplasmic sperm injection (ICSI) has transformed treatment of this type of severe male-factor infertility. Sperm can be retrieved for ICSI from either the epididymis or the testis, depending on the type of azoospermia. OBJECTIVES To evaluate the efficacy of the various surgical retrieval techniques for men with obstructive or non-obstructive azoospermia prior to ICSI. SEARCH STRATEGY We searched the Cochrane Menstrual Disorders and Subfertility Group Trials Register (November 2007), Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2007, Issue 4), MEDLINE (1966 to November 2007), EMBASE (1980 to November 2007), Biological Abstracts (1980 to November 2007), and reference lists of identified articles. SELECTION CRITERIA Randomised controlled trials (RCTs) comparing the effectiveness of different sperm-retrieval techniques in men with azoospermia prior to ICSI. Due to the lack of RCTs, non-randomised trials that used the participants as their own control were also considered in the review but their results were not included in the meta-analysis. DATA COLLECTION AND ANALYSIS Two review authors independently assessed trial quality and extracted data. Study authors were contacted for additional information. MAIN RESULTS The search was revised and re-run in November 2007. No new trials were located therefore the results of the updated review remain unchanged from those published in 2006. Two trials involving 98 men were included. The first small RCT had 59 participants and compared two epididymal techniques. The trial gave limited evidence that microsurgical epididymal sperm aspiration (MESA) achieved a significantly lower pregnancy rate (one pregnancy in 29 procedures compared with seven pregnancies in 30 procedures; OR 0.19, 95% CI 0.04 to 0.83) and fertilisation rate (OR 0.16, 95% CI 0.05 to 0.48) than the micropuncture with perivascular nerve stimulation technique. The other RCT comparing two testicular aspiration techniques (TSA) in 39 participants gave no statistically significant evidence for the superiority of the ultrasound-guided technique compared to the aspiration technique without ultrasound. TSA with ultrasound resulted in pregnancy in three out of 16 participants compared with four out of 23 participants (OR 1.10, 95% CI 0.21 to 5.74). AUTHORS’ CONCLUSION There is insufficient evidence to recommend any specific sperm retrieval technique for azoospermic men undergoing ICSI. In the absence of evidence to support more invasive or more technically difficult methods, the review authors recommend the least invasive and simplest technique available. Further randomised trials are warranted, preferably multi-centred trials. The classification of azoospermia as obstructive and non-obstructive appears to be relevant to a successful clinical outcome and a distinction according to the cause of azoospermia is important for future clinical trials.

Database: Medline

Author(s): Stalf, T; Schuppe, H-C; Henkel, R; Weidner, W; Schill, W-B; Tinneberg, H-R; Gips, H

Source: Andrologia; Jun 2003; vol. 35 (no. 3); p. 181-183

Publication Date: Jun 2003

Publication Type(s): Journal Article

PubMedID: 12780545

Available at Andrologia - from Wiley Online Library Science, Technology and Medicine Collection 2017

Database: Medline
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<td>107</td>
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<td>4</td>
<td>Medline</td>
<td>(PESA OR TESE).ti,ab</td>
<td>819</td>
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<td>5</td>
<td>Medline</td>
<td>exp &quot;SPERM RETRIEVAL&quot;/</td>
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<td>6</td>
<td>Medline</td>
<td>(1 OR 2 OR 3 OR 4 OR 5)</td>
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<td>((increase* OR high*) ADJ2 &quot;sperm DNA fragmentation&quot;).ti,ab</td>
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<td>8</td>
<td>Medline</td>
<td>(&quot;DNA Fragmentation&quot;).ti,ab</td>
<td>19464</td>
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<td>9</td>
<td>Medline</td>
<td>exp &quot;DNA FRAGMENTATION&quot;/</td>
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<td>26063</td>
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<td>(sperm).ti,ab</td>
<td>71968</td>
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<td>Medline</td>
<td>exp SPERMATOZOA/</td>
<td>63232</td>
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<td>Medline</td>
<td>(11 OR 12)</td>
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<td>Medline</td>
<td>(10 AND 13)</td>
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<td>15</td>
<td>Medline</td>
<td>(7 OR 14)</td>
<td>2036</td>
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<tr>
<td>16</td>
<td>Medline</td>
<td>(6 AND 15)</td>
<td>35</td>
</tr>
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<td>17</td>
<td>EMBASE</td>
<td>(&quot;Percutaneous epididymal sperm aspiration&quot;).ti,ab</td>
<td>165</td>
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<td>18</td>
<td>EMBASE</td>
<td>(&quot;Testicular sperm extraction&quot;).ti,ab</td>
<td>1375</td>
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19 EMBASE
"SURGICAL SPERM RETRIEVAL".ti,ab

20 EMBASE
(PESA OR TESE).ti,ab

22 EMBASE
exp "SPERM RETRIEVAL"/ OR 2387 exp "MICROSURGICAL EPIDIDYMAL SPERM ASPIRATION"/ OR exp "PERCUTANEOUS EPIDIDYMAL SPERM ASPIRATION"/ OR exp "TESTICULAR SPERM ASPIRATION"/ OR exp "TESTICULAR SPERM EXTRACTION"/

23 EMBASE
(17 OR 18 OR 19 OR 20 OR 22) 3433

24 EMBASE
((increase* OR high*) ADJ2 "sperm DNA fragmentation").ti,ab

25 EMBASE
exp "DNA FRAGMENTATION"/ 14971

26 EMBASE
(24 OR 25) 14994

27 EMBASE
(23 AND 26) 113

28 EMBASE
exp "TREATMENT INDICATION"/ 117886

29 EMBASE
(27 AND 28) 0