



MICROSCOPIC TESTICULAR SPERM EXTRACTION; PATIENTS IN OF NON-OBSTRUCTIVE AZOOSPERMIA WITH HISTPATHOLOGIC, CYTOGENETIC AND HORMONAL VARIATIONS.

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INTRODUCTION

Azoospermia, the complete absence of sperms in the ejaculate is found in 1% of normal males and 10-15% of infertile couples.¹ Management of male infertility has been entered in new era over last two decades after the introduction of multiple techniques for surgical sperms retrieval. The spectrum encompasses fine needle aspiration (FNA) of the testes, conventional testicular sperms extraction (TESE) and microscopic testicular sperm extraction (Micro-TESE).² Surgical sperm retrieval and subsequent use for ICSI/IVF offers an opportunity of fertility among male factor infertile couples.³ MicroTESE is a surgical procedure in which both the testes are incised and, under operating microscope, the

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ABSTRACT ... Azoospermia, the complete absence of sperms in the ejaculate is found in 1% of normal males and 10-15% of infertile couples. Surgical sperm retrieval (SSR) and use of sperms for ICSI/IVF offers an opportunity of parenting to the male factor infertile couples. Micro-TESE gives higher surgical sperms retrieval rates in those patients in whom the chances of sperm retrieval otherwise are very low. **Objectives:** To evaluate the outcome of Microscopic Testicular Sperm Extraction (Micro-TESE) in different patients groups of non-obstructive azoospermia, in terms of testicular volume, histopathology, hormones levels as well as cytogenetic variants. **Study Design:** Retrospectively reviewed. **Setting:** Urology Division, King Fahd Medical City, Riyadh in collaboration with King Abdullah Reproductive Medical Unit (RMU). **Period:** January 2011 to January 2016. **Material & Methods:** Fifty-four patients of primary and secondary infertility age range of 29 to 65 years who had undergone Microscopic Testicular Sperm Extraction (Micro-TESE). **Outcome measures:** Finding of sperm in testicular specimen extracted by microscopic testicular dissection. **Results:** Out of 54 patients, hormonal abnormalities were found in 45% patients and 65% had low volume testes. Abnormal histology was found in 23% patients and 9% had chromosomal abnormalities. Overall sperm retrieval rate in all groups was 33%. Sperm retrieval rate was 34 % in patients with small volume testes (<15ml), 42% patients with abnormal hormones (FSH), 33% patients with abnormal histology and 38% in patients with chromosomal abnormalities. Minor complications (small hematoma and orchalgia) were observed in two (3.7%) patients. **Conclusion:** Micro-TESE is a valid option for sperm retrieval in patients in which probability of sperm retrieval is otherwise very low.

Key words: Azoospermia, Infertility, Microscopic Testicular Sperm Extraction, Cytogenetics, Surgical Sperm Retrieval, Assisted Reproductive Techniques.

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more normal appearing tubules are extracted. They are then examined under the microscope in the operating room and if sperms are found, they are processed by the embryologist for use of IVF/ICSI in the same sitting or cryopreserved for the later use. Since its first introduction in 1999 by the Schlegel⁴, Micro-TESE has been reported to give higher surgical sperms retrieval rates than other methods.^{5,6} Where Micro-TESE has revealed positive sperms retrieval in normal histologic and normal cytogenetic groups of patients, there has been multiple reports that sperms were retrieved in azoospermic patients even with abnormal histopathology like sertoli cell only syndrome and maturation arrest as well as in abnormal cytogenetics like Klinefelter's syndrome.⁷

European guidelines has also recommended MicroTESE as a surgical sperm retrieval technique in patients with non-obstructive azospermia.⁸ Complications of surgical sperm retrieval are less common and minor. It includes persistent testicular pain, infections or hematoma.⁹ Because of less number of retrieved sperms by micro-dissection, ICSI is preferred method for fertilization instead of IUI or IVF.^{10,11} The objective of current study was to evaluate the outcome of MicroTESE procedure in various groups of patients with non-obstructive azoospermia, in our institution.

MATERIALS AND METHODS

Fifty-four (54) consecutive patients of primary infertility and azoospermia, with mean age range 29 to 65 years (mean 36.9 years) were included in the study. Patients with histological abnormalities, genetic abnormalities, patients with previous chemotherapy were included in the study. Histological abnormalities included sertoli cell only syndrome (SCOS), maturation arrest, hypospermatogenesis and germ cell aplasia. Genetic abnormalities found were Y-chromosome microdeletion and Klinefelter's syndrome. A detailed history (potency, type and duration of infertility, previous interventions for sperm retrieval,) and physical examination (testicular volume, presence of vas deference, signs of hypogonadism) of all patients was performed. Semen analysis and hormonal assay (serum FSH, LH, Testosterone and Prolactin levels) were performed. Infection serology (for Hepatitis B&C and HIV) was done and positive cases were excluded from the study as no separate cryopreservation facility is available in our center for the infected patient's sperms. Cytogenetic studies (karyotyping) were performed for all patients with azoospermia. Patients with good volume testes and normal hormone levels were subjected to micro-TESE only if they had previously failed procedures (for example FNA-biopsies of the testes and/or conventional TESE). Whereas, the patients with negative predictive factors (such as small testicular volumes and/or higher levels of serum FSH) were directly subjected to Micro-TESE.

All these men underwent Microscopic Testicular

Sperm Extraction (Micro-TESE) from January 2011 to January 2016 by certified Andrologist. The Micro-TESE was performed as a day procedure. The testes were approached through a midline scrotal incision and delivered. Tunica albugenia was incised longitudinally. Strict hemostasis ensured with bipolar diathermy. Under 25X magnification microscope, micro-dissection of seminiferous tubules with healthier appearance was performed and specimens obtained. Specimens were examined in the operating room under a microscope for the presence of sperms, as well as delivered immediately to embryology lab for examination as well as processing of sperms for ICSI cycle or cryopreservation by the embryologist. The success of sperm retrieval is defined as the recovery of at least one spermatozoon. The data were collected from the hospital database and analyzed through SPSS. The study variables were overall sperms retrieval rate, distribution of sperms retrieval rates in patients with histo-pathological abnormalities of testes, cytogenetic abnormalities, hormonal levels, and complications of the procedure. ANOVA and chi-square tests were applied for data analysis.

ETHICAL CONSIDERATION

The current study belonged to one of the exempt categories for research, as per rules of the Institutional Review Board, and exemption letter was issued. "Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects".

All patients given informed consent of the procedure. The privacy and confidentiality of the patients were strictly observed.

RESULTS

Out of fifty four patients, sperms were retrieved in 18 (33.3%) patients. The distribution of different variables among the whole study group and

means + standard deviations of numerical variables were as under (Table-I Table-II);

	FSH	Cytogenetics	Histopathology
Normal	30	49	42
Abnormal	24	05	12
Total	54	54	54

Table-I. Descriptive statistics

Sperms were retrieved in patients with normal as well as abnormal histopathological and cytogenetic variants. Histological abnormalities found were Sertoli cell only syndrome (SCOS), maturation arrest, hypospermatogenesis and germ cell aplasia. Genetic abnormalities found were Y-chromosome microdeletion (patient) and Klinefelter’s syndrome. Sperm were retrieved both in patients with normal and high FSH levels (which is otherwise a negative predictor for sperm

retrieval). However, difference between sperm retrieval rate was not statistically significant (Table-III).

In patients with abnormal cytogenetic, two patients with Klinefelter’s syndrome were found to have sperms with micro-TESE.

Sperms were retrieved in one patient who had undergone orchiectomy and adjuvant chemotherapy for testicular cancer. Sperms were also retrieved from 37 % of patients with atrophic testes (volume <5ml). Two (3.7%) patients developed complications. One got scrotal hematoma and other had orchalgia for three post-operative months. Both were managed conservatively.

	Overall (n:54)		Sperms positive group (n:18)		Sperms negative group (n:36)	
	Mean	S.D	Mean	S.D	Mean	S.D
Age (years)	36.91	7.354	38.44	8.33	36.14	6.808
Duration of inf.(years)	7.2	4.364	7.22	4.110	7.22	4.543
Testicular Volume(ml)	12.28	4.603	11.89	4.993	12.47	4.456
FSH(IU/L)	16.25	14.737	20.59	16.469	14.09	13.513

Table-II. Means & S.D of variables & Distribution among groups

n:54	Overall	Normal FSH	Raised FSH	Normal Histopathology	Abnormal Histopathology	Normal Cytogenetics	Abnormal Cytogenetics
Sperms Found	18 (33.3%)	08 (26.07%)	10 (41.7%)	14 (33.3%)	04 (33.3%)	15 (30.6%)	03 (60%)
Sperms not found	36 (66.7%)	22 (73.3%)	14 (58.3%)	28 (66.7%)	08 (66.7%)	34 (69.4)	02 (40%)
n:54	54	30	24	42	12	49	05

Table-III. Sperm retrieval rates in different groups

DISCUSSION

Micro- TESE has been known as a procedure for men with non-obstructive azoospermia (NOA)⁶, with more in sperm retrieval than a single biopsy or multiple random biopsies.¹²⁻¹³ Multiple reports have been published about Micro-TESE outcome. Tahsin, Turunc and colleagues in 2010 compared conventional TESE and Micro-TESE in their study and described 20.7% sperm retrieval rate in patients in whom Micro-TESE was done as primary procedure.⁴ Karel et all in 2006 reported SSR rate of 35%) of the men who were undergone

Micro-TESE in their center. The per couple take home baby rate in the same study, if sperm was retrieved, was 24%.³ Correlation between sperm retrieval rate has been found to be associated with multiple factors and predictors.¹⁴⁻¹⁵ Tsujimura et al. reported that SRR by micro-TESE for patients with sertoli cell only syndrome was 22.5%, whereas by conventional TESE it was 13%.¹³ In 2010, Ishikhawa reported an interesting predictor that was number of procedures and learning curve of operating surgeon. In their first 50 cases of MicroTESE, sperm retrieval rate was

32% that increased to 44 % in next 50 cases.⁵ Another predictor of sperm retrieval is FSH levels of the patient. Micro-TESE is mostly performed as last available procedure in most of the centers. A mental strain for a sensitive couple is expected and so, a realistic approach is required by the surgeon as well as the couple, keeping in mind all the possible predictors of positive sperms retrieval. Elevated FSH levels have been associated with a low probability of the retrieval of spermatozoa in men¹⁶ using random biopsy TESE techniques. Serum FSH is an indirect reflection of the spermatogenic function and histology of the testis as a whole. Therefore, FSH may predict the presence of sperm at random biopsy using conventional TESE techniques.¹⁷⁻²⁰ To increase the probability of sperm retrieval, various pre- treatments have also been worked out. The pretreatment with beta-HCG has also been studied. The Leydig cells of the testis can respond positively to exogenous beta-hCG even under hypergonadotropic conditions. HCG-based hormonal therapy prior to a second micro-TESE attempt is effective in men with hypospermatogenesis.²¹

CONCLUSION

Micro-TESE is safe and established procedure for SSR. Sperm can be retrieved in men with NOA, including Klinefelter's syndrome (KS), prior history of chemotherapy and cryptorchidism. Sperm retrieval rates are predicted by factors like histology of testis and serum FSH levels. It may be expected to increase with pre-op hormone manipulation as well increased number of procedures. Very few and minor complications are encountered and can be managed conservatively.

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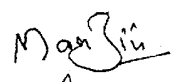
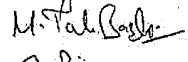
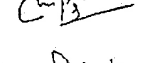
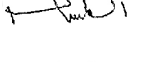
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5	M. Yahya Alrawi	Embryologist, Evaluated the shades and data collection.	