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Role of Serum Follicle-Stimulating Hormone Level as Predictor of Sperm Retrieval in Patients with Non-Obstructive Azoospermia

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Abstract

The aim of this study was to determine the predictive value and use of noninvasive, pre-operative estimation of serum follicle-stimulating hormone (FSH) on sperm retrieval rate (SRR) during microdissection testicular sperm extraction (mTESE) in patients with non-obstructive azoospermia (NOA).

Materials and Methods*:* A retrospective review of the charts of 74 patients (mean age of 36.7±6.7 years) with NOA who underwent mTESE was performed. Pre-operative serum levels of FSH, total testosterone, luteinizing hormone (LH), estradiol, prolactin and mTESE results were analyzed. Patients were divided into two groups according to the mTESE results: Group A (positive sperm retrieval) and Group B (negative sperm retrieval).

Results: Sperm was retrieved from 29 patients (positive SRR 39%). The mean serum FSH levels were 24.83±10.09 mIU/mL in Group A and 31±4.24 mIU/mL in Group B, without statistically significant differences between the two groups (P>0.05). In addition, there were no observed statistically significant differences between the two groups regarding serum LH, total testosterone, estradiol and prolactin levels.

Conclusion*:* The study found that pre-operative measurement of serum FSH level has no significant predictive value on SRR at mTESE in men with NOA.(**International Journal of Biomedicine. 2019;9(1):35-38.**)

Key Words: non-obstructive azoospermia • microdissection testicular sperm extraction • follicle-stimulating hormone • male infertility

Abbreviations

ART, assisted reproduction technologies; **FSH**, follicle-stimulating hormone; **ICSI**, intra-cytoplasmic sperm injection; **LH**, luteinizing hormone; **mTESE**, microdissection testicular sperm extraction; **NOA**, non-obstructive azoospermia; **SRR**, sperm retrieval rate.

Introduction

Infertility is defined as failure to achieve a clinical pregnancy following 12 months of regular, unprotected sexual intercourse.[1] It has been reported to affect 15% of couples, with a male factor contribution to the fertility problem in almost 50%.[2,3] The complete absence of sperm from the ejaculate is called *azoospermia* and occurs in 1% of all men and in 10%–12% of the infertile male population.[4] Azoospermia can be classified as obstructive and non-obstructive depending on the cause of it. NOA, which is caused by testicular failure, accounts for 60% of all cases of azoospermia and represents the most challenging case scenario.[5]

With advances in ART and the success of ICSI of surgically retrieved sperm, couples with NOA can have their own children.[6] There are different surgical procedures to retrieve sperm from patients with NOA, including percutaneous testicular biopsies, open conventional testicular biopsies and mTESE. In NOA patients, sperm can be found in small islands following extensive dissection of seminiferous tubules with SRR approaching 40%-50% with mTESE.[7]

A thorough medical history and examination are essential for proper evaluation and management of NOA

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patients. Before attempting sperm retrieval, use of pre-operative, noninvasive parameters to predict the success of finding sperms is helpful. There have been several studies in the literature with controversial predictive values about the use of non-invasive parameters and SRR during mTESE. FSH has been used as a marker for sperm production and considered one of the important pre-operative serum parameters in evaluating NOA patients. In the literature, elevated levels of serum FSH are postulated to have an inverse effect on finding sperm following sperm retrieval procedures.[8,9] In this study, the role of pre-operative, noninvasive measures of serum FSH in prediction of a successful sperm retrieval in patients with NOA who underwent mTESE procedures is evaluated.

Materials and Methods

We performed a retrospective review of the charts of 74 patients with NOA who underwent mTESE between August 2015 and December 2018 and met the inclusion criteria for this study. Enrolled subjects were required to have at least two separate azoospermia semen analyses of normal volume, palpable vas deferens on both sides and no history of sexually transmitted diseases, vasectomy or prior inguinal hernia repair. Data on reproductive history, a physical examination, semen analysis, and hormonal profile were analyzed. Serum FSH levels were determined by ELISA with a normal reference range of FSH between 1.5 mIU/mL and 15 mIU/mL. Based on serum FSH levels, patients were divided into Group 1 (FSH≤15) and Group 2 (FSH>15). Semen analysis was performed concurring with WHO criteria (WHO laboratory manual for the examination and processing of human semen; 2010).

mTESE was performed under general anesthesia on all enrolled subjects. A small midline scrotal incision was made to allow easy access to both testes. Patients were examined under anesthesia for testicular size and consistency, and the most promising of the two testicles was brought out first after dissecting the dartos muscle and opening the tunica vaginalis. The tunica albuginea was then opened in a horizontal plane under the operating microscope using a No.15 blade. Initial inspection of the exposed seminiferous tubules was performed, followed by bivalving the testicle and exposing the deep compartment. The seminiferous tubules were then thoroughly and systematically examined for opaque and dilated tubules. Identified tubules were then harvested with forceps and put in a small tube filled with HEPES-buffered sperm medium and handed over to the IVF lab. An embryologist in the IVF lab examined the harvested testicular biopsies for presence of sperm. If sperms were identified and enough for freezing and subsequent ICSI, hemostasis was achieved with bipolar diathermy and closure of the tunica albuginea with interrupted absorbable monofilament suture was performed. Closure of tunical vaginalis was performed, followed by placing the testicle back into the hemiscrotum and closure of dartos muscle, fascia and scrotal skin. However, if no sperm was identified, the same technique was carried out on the contralateral testicle.

Statistical analysis was performed using statistical software package SPSS version 17.0 (SPSS Inc, Chicago, IL). Data are expressed as mean±SD. Inter-group comparisons were performed using Student's t-test. A probability value of $P<0.05$ was considered statistically significant.

The study was approved by the Qassim University Ethics Committee. Written informed consent was obtained from all the participants.

Results

A total of 74 patients with NOA (mean age of 36.7±6.7 years) were enrolled in this study and underwent mTESE as described in the methodology section. The baseline hormonal profiles showed in Table 1.

Table 1.
The baseline hormonal profiles of study patients

Variable	Mean±SD
Age, yrs	36.7 ± 6.7
Estradiol, pg/mL	101.56±42.37
FSH, mIU/mL	31±4.24
LH, mIU/mL	13.5±3.54
Total Testosterone, ng/mL	12.87±3.55
Prolactin, mIU/mL	9.83±5.91

Sperm was retrieved from 29 patients (positive SRR 39%) out of 74 in this cohort. There were 29 patients in Group A (positive sperm retrieval) and 45 in Group B (negative sperm retrieval). There were no statistically significant differences between the two groups with regard to age. The mean ages of Groups A and B were 37.86±6.83 and 35.89±5.90, respectively ($P>0.05$).

The mean serum FSH levels were 24.83±10.09 mIU/mL in Group A and 31±4.24 mIU/mL in Group B, without statistically significant differences between the two groups ($P>0.05$). In addition, there were no observed statistically significant differences between the two groups regarding serum LH, total testosterone, estradiol and prolactin levels (all *Ps*>0.05) (Table 2).

Table 2.
Age and serum hormones in patients of Group A and Group B

Variable	Group A	Group B	*P*-value
Age, yrs	37.86±6.83	35.89±5.90	>0.05
Estradiol, pg/mL	102.25±25.50	107.05±49.72	>0.05
FSH, mIU/mL	24.83±10.09	31±4.24	>0.05
LH, mIU/mL	14.73±6.26	13.5±3.54	>0.05
Total testosterone, ng/mL	12.43±2.84	12.85±4.12	>0.05
Prolactin, mIU/mL	10.27±5.16	11.21±6.53	>0.05

Discussion

From the first successful ICSI in 1994 by use of surgically retrieved sperm, finding testicular sperms when combined with ICSI offers men with NOA a chance to have

their own children.[10,11] For couples pursuing surgical sperm retrieval and the IVF/ICSI option, a discussion regarding the appropriate expectations and outcomes of their specific clinical scenario is crucial.[12] Although there are no specific clinical findings or investigations that accurately predict the finding of sperm in NOA patients, some clinical factors have been found that affect the sperm retrieval in these patients. These factors include genetic testing (Y chromosome microdeletions and chromosomal abnormalities), testicular biopsy and testicular histology. Testicular histology in NOA patients may reveal hypospermatogensis, maturation arrest, both early and late, and Sertoli Cell Only syndrome (SCOS).[13,14] Patients with SCOS carry the lowest SRR during mTESE.

One of the important pre-operative parameters obtained during evaluation of men with azoospermia is serum FSH. Overall, the higher the serum FSH level, the lower the rate of surgically retrieved sperms. Since the successful finding of sperms within some islands of seminiferous tubules in NOA patients, along with high FSH levels, some authors have not found any adverse relationships between SRR and serum FSH level. However, some other researchers have observed a small relationship between FSH levels and SRRs, with a decrease in SRRs as FSH levels increase. Ramasamy and colleagues reported SRR of 51% with serum level of FSH of less than 15I U/mL, 60% SRR with serum FSH value between 15 and 30 IU/mL, 67% SRR with FSH levels of 31–45 IU/mL and 60% SRR with FSH levels more than 45 IU/mL.[15] Lower SRRs have been reported in men with higher FSH levels, and different studies [16,17] have reported different SRRs, resulting in conflicting associations between serum FSH levels and SRRs. In this study, FSH levels have not predicted the success of sperm retrieval during mTESE in NOA patients. There was no significant association between serum LH, total testosterone, prolactin or estradiol levels and sperm retrieval rates.

Serum inhibin-B has been suggested as a direct measure of sertoli cell function and an indirect marker of active spermatogenesis.[18] In patients with SCOS, inhibin-B has been found undetectable despite normal testosterone levels.[19] Studies comparing inhibin-B to FSH as a predictor of sperm retrieval have demonstrated that inhibin-B has a sensitivity of 75.86% and a specificity of 80.85%, compared to 64.78% and 84.69% for FSH.[20] In the literature, some studies have shown a superior predictive value of inhibin-B over serum FSH while others have demonstrated similar predictive values. The combination of the two tests will ultimately give a better predictive value than doing only one of them.[21,22]

Q Yang et al. performed a systematic review and meta-analysis for FSH as a predictor of sperm retrieval in NOA. They did notice variations in the diagnostic value of the serum FSH level with patient age and region of residence. FSH was shown to have more diagnostic value if the patients are younger and of East Asian descent and concluded that FSH had moderate diagnostic value as an independent predictor for SRR in patients with NOA.[23]

The limitations of this study include retrospective design, small sample size and no information on the final histologic results of the testicular biopsies. Thus, a well-designed prospective study is needed and may provide more insights into the role of serum FSH and other pre-operative, noninvasive parameters in prediction of sperm retrieval during mTESE in patients with NOA. Combining serum FSH level with other pre-operative, noninvasive parameters in future research may add more diagnostic and therapeutic options to infertile men diagnosed with NOA.

Conclusion

Couples with NOA can have their own biological children when sperms are successfully retrieved from testicles. In the literature, there are conflicting results on the role of pre-operative, noninvasive parameters in prediction of sperm retrieval during mTESE. In this study, there was no statistically significant difference in serum FSH levels between NOA patients who have sperm retrieved and those who have no sperm retrieved.

Disclosures

None

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