The Association between Serum Follicle-Stimulating Hormone Levels and the Success of Microdissection Testicular Sperm Extraction in Patients with Azoospermia

Mehmet Erol Yildirim,[1] Akif Koc,[2] Ikbal Cekmen Kaygusuz,[3] Hüseyin Badem,[4] Omer Faruk Karatas,[1] Ersin Cimentepe,[1] Dogan Unal[5]

[1]Department of Urology, Turgut Ozal University, Faculty of Medicine, Ankara 06510, Turkey.
[2]Department of Urology, Balıkesir University, Faculty of Medicine, Balikesir 10310, Turkey.
[3]Department of Gynecology and Obstetrics, Turgut Ozal University Faculty of Mediine, Ankara 06510, Turkey.
[4]Department of Urology, Yüksek İhtisas Training and Research Hospital, Ankara 06520, Turkey.
[5]Department of Urology, Hacettepe University Faculty of Medicine, Ankara 06520, Turkey.

Corresponding Author:
Mehmet Erol Yildirim, MD
Department of Urology, Turgut Ozal University School of Medicine, 06510, Yenimahalle, Ankara, Turkey.

Tel: +90 312 2035221
Fax: +90 312 2213670
E-mail:doctorerol@yahoo.com

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Purpose: To evaluate the predictive power of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, testicular biopsy histology and male age were evaluated with respect to the success of sperm retrieval in a microdissection testicular sperm extraction (microTESE) procedure, pregnancy and live birth rates.

Materials and Methods: We examined the data of 131 infertile men with non-obstructive azoospermia, who have undergone microTESE operation. The men were classified into two groups based on serum follicle-stimulating hormone (FSH) levels ≤ 15 mIU/mL (group 1) and > 15 mIU/mL (group 2).

Results: Group 1 consisted of 59 patients (mean age 36.2 ± 6.2 years) and group 2 consisted of 72 (mean age 38.8 ± 7.4 years) patients. Sperm retrieval and pregnancy rates were 66.1% and 16.9% in normal FSH group, respectively. These parameters were higher than those of men with FSH > 15 (43% and 8.3%, respectively). Only 128 patients had histopathological diagnosis. Sperm was retrieved from 12/30 (40%) patients with maturation arrest, 9/29 (31.03%) patients with seminiferous tubules atrophy, 14/40 (35%) patients with sertoli cell only syndrome and 13/13 (100%) of patients with hypospermatogenesis. There was no statistically significant difference in pathological diagnosis between pregnancy and live birth rates.

Conclusion: These results demonstrate that there is a significant difference with sperm retrieval, pregnancy rates and live birth rates comparing the FSH levels. Histopathological findings did not associate with successful microTESE, pregnancy rates and live birth rates.

Keywords: infertility, male; microdissection; sperm retrieval; testicular diseases; azoospermia; spermatogenesis.

INTRODUCTION

Infertility is defined as the inability to conceive a child after one year of regular unprotected intercourse.[1] Infertility is a major health problem that effects approximately 15% of couples, and nearly 50% of this is because of male infertility.[2] There are many reasons for male infertility, but testicular factors play the leading role. Assisted reproductive techniques, such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), offer the possibility of fertilizing oocytes even if only a small number of spermatozoa are found in the ejaculate. In cases of azoospermia, sperm is obtained from the epididymis and testes by surgical procedures. Microdissection testicular sperm extraction (microTESE) is performed to recover sperm from azoospermic patients and was shown to be successful even in testes with only small islets of spermatogenesis.[3] However, every failed microTESE-ICSI procedure exposes the couple to an emotional and financial burden. It becomes increasingly important to predict the success of sperm retrieval using non-invasive parameters before the attempted treatment. There are many studies about using a patient's hormonal status and previous testicular biopsy histology to predict the success of microTESE in recent years.[4] In our study, the predictive power of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, testicular biopsy histology and male age were evaluated with respect to the success of sperm retrieval in a microTESE procedure, pregnancy and live birth rates.

MATERIALS AND METHODS

Study Subjects

The data of 131 patients with non-obstructive azoospermia who have undergone microTESE between January 2006 and November 2012 were examined. Inclusion criteria were, no sperm found in the ejaculate, existence of bilateral vas deferens and no history of genital infection, surgery or vasectomy. Azoospermia was confirmed via analysis of two different semen analyses according to World Health Organization (WHO) criteria.[5] A semen sample was also collected on the day of microTESE. All hormonal levels were determined by the chemiluminescent immunoassay (Immulite 2000, Siemens diagnostics, Los Angeles, CA, USA) method. The reference range of FSH was 1.5-15 mIU/mL, LH was 4-8.6 mIU/mL and testosterone was 245-1600 ng/dL.

All patients underwent microTESE with local anesthesia. After a midline scrotal incision, we pushed out the biggest testis and opened the tunica vaginalis. After the visualization of the tunica albuginea, the remainder of the procedure was performed under × 20 magnification with an operative microscope. Small samples were excised from the testis. Each sample was examined immediately by the embryologist under × 200 magnification. If no spermatozoa were identified in the initial sample, the incision of the tunica albuginea was expanded and subsequent samples were taken from the larger and more opaque tubules, if needed, from the contralateral testis. The procedure stopped when enough spermatozoa were retrieved or when further dissection would jeopardize the testicular blood supply. A sample was taken for histopathological investigation from each procedure. The patients were divided into two groups based on their serum FSH levels; ≤ 15 mIU/mL (group 1) and > 15 mIU/mL (group 2). The patients were also classified according to their testicular pathology, such as maturation arrest, testicular atrophy, sertoli cell only syndrome or hypospermatogenesis. The groups were compared with regards to sperm retrieval, pregnancy and live birth rates. Informed consent was taken from all patients in order to use their data. Also, ethics approval was obtained from our Institutional Ethics Committee.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 16.0. Independent groups were compared using the Mann Whitney *U* test and group rates were compared by the student's *t*-test. *P* values of < .05 were considered as statistically significant.

RESULTS

The average age of patients undergoing microTESE was 37.72 ± 5.8 (range, 26-57) years. There were 59 patients in group 1 and 72 patients in group 2. The mean age of group 1 and 2 were 36.2 ± 6.2 and 38.8 ± 7.4, respectively. There were statistically significant differences between both groups with regards to sperm retrieval (*P* = .008), but not to pregnancy rates (*P* = .136) nor live child delivery rates (*P* = .136) (**Table 1**).

The mean serum FSH levels were 17.4 ± 16 (95% confidence interval [CI]: 13.6-21.3) mIU/mL and 24.1 ± 15.8 (95% CI: 20.1-28.2) mIU/mL in the sperm retrieved and non-sperm retrieved groups. There was a statistically significant difference in serum FSH levels (*P* = .03) between sperm retrieved and non-sperm retrieved groups. However, there were neither statistically significant differences in serum FSH levels between pregnancy and non-pregnancy groups (*P* = .655) nor between child delivered and non-child delivered groups (*P* = .655) (**Table 2**). With regards to the patient's ages, there were no statistically significant differences between sperm retrieved and non-retrieved groups (*P* = .66), child delivered and non-child delivered groups (*P* = .457) and pregnancy and non-pregnancy groups (*P* = .457) (**Table 2**).

There is a negative correlation between sperm retrieval and both serum FSH levels and patient ages (r = -0.207, *P* = .018 and r = -0.159 *P* = .07, respectively). We could collect only 128/131 patients' data regarding their testicular histology. According to these data, there were no statistically significant difference between histological findings and sperm retrieval (*P* = .178), pregnancy rate (*P* = .198), or child delivered groups (*P* = .063) (**Table 3**). Also there was only a positive correlation between hypospermatogenesis and sperm retrieval (r = .281, *P* = .001).

DISCUSSION

Table 1. Sperm retrieval, pregnancy and live birth rates compared between two groups.*

Variables	Serum FSH Levels (mIU/mL)		*P* Value
	≤ 15	> 15	
Sperm retrieved	38/59 (66.1)	31/72 (43)	.008
Pregnancy rate	10/59 (16.9)	6/72 (8.33)	.136
Live birth rate	10/59 (16.9)	6/72 (8.33)	.136

* Data are presented as no. (%).

About 15% of couples have infertility problems.[2] The chances of having a pregnancy increases from the first month (25%) to a year (90%).[6] Male factors play an important role in 50% of infertile couples.[7] Today, microTESE plus ICSI gives the chance to have a baby to infertile couples.[8] Many infertile couples who were considered desperate cases in past years may now have children with the rise of microTESE and ICSI techniques in clinical practice. While there are significant contributions of microTESE procedures to infertility, it has a particular organic and psychological morbidity due to its invasiveness. For this reason, predictive markers are needed for the clinician to make decisions about the first or repetitive microTESE. Most of the past studies have focused specifically on testicular histology and serum FSH levels to make the decision about microTESE.

The present study focuses on whether any association between serum FSH, LH and testosterone levels, testicular histology and sperm retrieval, pregnancy and live birth rates. Our threshold level for FSH was 15 mIU/mL. Some reports mentioned that we can't retrieve sperm by microTESE with higher serum FSH levels because of existing testicular atrophy.[9] Ezeh and colleagues showed a weak correlation between serum FSH level and successful microTESE.[10] No matter how high the serum FSH level that, there is always a chance to retrieve sperm.[11] In our study, the sperm retrieval rates at serum FSH normal group and serum FSH > 15 mIU/mL group were 64.4% and 43%, respectively, and pregnancy and live birth rates were 16.9% and 8.33%, respectively. Even if there was a statistically significant difference between sperm retrieval rates and serum FSH levels (P = .008), there was not such a correlation between serum FSH levels and pregnancy and live birth rates. Ramasamy and colleagues reported that sperm retrieval rates in the groups with serum FSH values of 15-30 mIU/mL, 31-45 mIU/mL and > 45 mIU/mL were 60%, 67% and 60%, respectively, and this was, surprisingly, higher than the normal serum FSH (51%) group.[4] Therefore, according to Ramasamy and colleagues, we can retrieve sperm by microTESE even despite FSH values of 2-3 times higher than normal. Otherwise, pregnancy (46%, 50%, 52% and 46%, respectively) and live birth rates (38%, 45%, 44% and 36%, respectively) were similar in both serum FSH normal and higher groups.[4] Bohring and colleagues showed that both serum FSH and inhibin B are relevant with spermatogenesis. But they had not concluded these hormones to be definite predictive factors because despite the abnormal levels of these hormones, successful microTESE were performed.

Many studies have shown that the histopathology of testes to be the best predictor concerning the retrieval of sperms in microTESE.[13] But, there is some controversy as to whether a random sampling may not represent the inherent heterogeneity, because augmentation of the sampling may cause inflammatory changes, hematoma, parenchymal fibrosis or permanent devascularization of the testis.[14] Tunç and colleagues reported a 42.1% sperm retrieval rate at germinal aplasia, and the best (83.3%) at hypospermatogenesis.[15] Su and colleagues reported 24% sperm retrieval rates at sertoli cell only syndrome (SCOS) and higher rates were 79% at hypospermatogenesis.[16] Tournaye and colleagues reported 67% sperm retrieval rates at SCOS, 82% at maturation arrest and 100% at hypospermatogenesis.[17] Our sperm retrieval rates were 35% at SCOS, 40% at maturation arrest, 31.03% at seminiferous tubules atrophy and 100% at hypospermatogenesis, which are consistent with current literature. As we grouped patients according to the histopathologic diagnoses, there was no correlation with sperm retrieval rates, pregnancy rates and live birth rates except in patients with hypospermatogenesis. The main paradox of the testis biopsy is the doubt about the histology of the rest of the testis.

Evaluation of serum FSH levels with testis histology can be a predictor for sperm retrieval in microTESE. There was a correlation between low serum FSH and hypospermatogenesis at sperm retrieval; on the other hand, there was not any correlation between maturation arrest and SCOS.[3] In another study, a group of 17 men with hypospermatogenesis, 22 men with obstructive azoospermia and 29 men with normal spermatogenesis in whom sperm was retrieved successfully with microTESE, there was no difference in serum FSH levels.[18] Maturation arrest (50%) was the common pattern in the serum FSH normal group, and otherwise SCOS (51.1%) was the main group in the higher serum FSH group in our study.

Table 2. Comparison of FSH levels and age according to the sperm retrieval, pregnancy and live birth rates.

Variables	Sperm Retrieval			Pregnancy Occurrence			Child Delivery		
	Yes (n = 69)	No (n = 62)	*P* Value	Yes (n = 69)	No (n = 62)	*P* Value	Yes (n = 69)	No (n = 62)	*P* value
Serum FSH (mIU/mL)	17.48 ± 6.02	24.1 ± 15.8	.03	15.9 ± 14.3	21.2 ± 16.4	.655	15.9 ± 14.0	21.2 ± 16.4	.652
Age (years)	37.5 ± 5.5	38.5 ± 7.8	.66	37.2 ± 5.9	38.1 ± 6.7	.457	37.4 ± 6.2	38.2 ± 6.6	.457

Table 3. Classification of sperm retrieval, pregnancy and live birth rates according to the histopathological findings.

Histopathology	Number	Sperm Retrieved	Pregnancy Rate	Live Birth
Maturation arrest	30	12	1	1
Seminiferous tubules atrophy	29	9	2	2
Sertoli cell only syndrome	40	14	3	3
Normal histology	16	14	5	3
P Values	-----	.178	.198	.063

CONCLUSION

Sperm retrieval, pregnancy and live child birth chances are better in serum FSH normal patients when compared to the serum FSH higher groups; however, statistical analyses showed no significant difference between both FSH groups concerning these three parameters. Even though there is a relationship between sperm retrieval, pregnancy and live birth rates, and hypospermatogenesis, there are not statistically significant differences from the other histopathological diagnoses.

CONFLICT OF INTEREST

None declared.

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