



Surgical sperm collection in Infertile Male with High FSH

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Background

Elevated FSH levels indicate a problem with spermatogenesis, however it does not guarantee that sperm cannot be retrieved from the testis. Serum FSH is an indirect reflection of the global (spermatogenic) function and histology of the testis as a whole. FSH may predict successful sperm retrieval at conventional testicular sperm extraction (TESE). FSH may reflect the predominant pattern of spermatogenesis, but it may not reflect isolated areas of spermatogenesis within the testis. Hence micro-TESE becomes a more useful method for successful sperm collection.

Introduction

Azoospermia is defined as absence of sperm in the ejaculate, it may occur due to obstruction in the reproductive tract (OA) or due to inadequate sperm production (NOA).

Although azoospermia affects 2% of the general population, non-obstructive azoospermia (NOA) is observed in 5% to 15% of men undergoing infertility evaluations and accounts for two-thirds of azoospermic cases.

Assisted reproductive technology has overcome this challenge to achieving a family, surgical sperm collection (SSC) and subsequent intracytoplasmic sperm injection (ICSI) offers couples the chance of having their own biological children.

Surgical sperm retrieval is highly variable and dependent on the levels of follicle stimulating

hormone at initial evaluation and its role in predicting success of surgical sperm retrieval has been researched extensively. Its clinical implications include determining the critical cut off value for FSH results when counselling clients for surgical sperm retrieval and ICSI.

However, while elevated FSH levels can sometimes indicate a problem with spermatogenesis, it does not guarantee that sperm cannot be retrieved from the testis.

Surgical sperm collection can be successful in men with non-obstructive azoospermia and high FSH levels although success rates vary.

While some studies suggest a correlation between higher FSH levels and lower sperm retrieval rates, particularly with larger testicular volumes, other demonstrate that even with high FSH, sperm retrieval

is possible using methods like micro-TESE.

Serum FSH is an indirect reflection of the global (spermatogenic) function and histology of the testis as a whole. Therefore, FSH may predict the presence of sperm at random biopsy using conventional TESE.

FSH may reflect the predominant pattern of spermatogenesis, but it may not reflect isolated areas of spermatogenesis within the testis.

Hence micro-TESE becomes a more useful method

for successful sperm collection. We critically appraise available literature in terms of methodology and outcomes, to determine whether high pre-treatment FSH precludes successful sperm collection in azoospermic males with non obstructive azoospermia.

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Discussion

Micro-TESE provides a better representation of testicular histology to support higher sperm retrieval rates, however the opinion that micro-TESE has lesser effect on testicular function than random biopsies from TESE because far less testicular tissue is removed is debatable.

However, contrary to previously reported studies testicular sperm retrieval rates were maintained even with markedly elevated FSH values.

Study 1

High serum FSH levels in men with non-obstructive azoospermia does not affect success of micro-dissection testicular sperm extraction.

Objective:

To evaluate the outcomes of microdissection sperm extraction (micro TESE) in patients with high FSH

Patients:

Seven hundred and ninety two men with non obstructive azoospermia

Interventions:

Micro-TESE followed by intracytoplasmic sperm injection (ICSI) was performed. The men were classified into four groups based on serum FSH levels: <15, 15–30, 31–45, and >45 IU/mL.

Outcome measures:

Sperm retrieval, clinical pregnancy and live birth rates. Testicular sperm were successfully retrieved in 60% of the men.

Sperm retrieval rates in the groups of men with FSH values 15–30, 31–45, and >45 IU/mL was 60%, 67%, and 60% respectively; this was higher than the group of men with FSH < 15 (51%).

The mean FSH in the group that failed to retrieve sperm (20.0 IU/mL, 95% CI 17.5–20.3) was not significantly different ($P=.24$) from the group with successful retrieval (18.8 IU/mL, 95% CI 18.7–21.3).

Of those men who had sperm retrieved, clinical pregnancy and live birth rates were similar in the four groups (46%, 50%, 52%, 46% and 38%, 45%, 44%, 36%, respectively).

Ranjith et al admitted that the relationship between FSH and spermatogenesis was not straight forward in men with NOA as they identified 3 men with FSH > 90 iu/ml in which successful sperm retrieval was seen.

They admitted with surprise greater odds of finding sperm with micro-TESE with pre-operative FSH values ≥ 15 iu/l compared with normal values.

They submitted that azoospermic males with normal FSH values are a clinically distinct subset where there was a higher prevalence of chromosomal abnormalities and Y chromosomal microdeletions compared to other patients with NOA (45% vs 17%); $P < 0.001$ with concomitant lower sperm retrieval rates (41% vs 60%); $P=0.05$

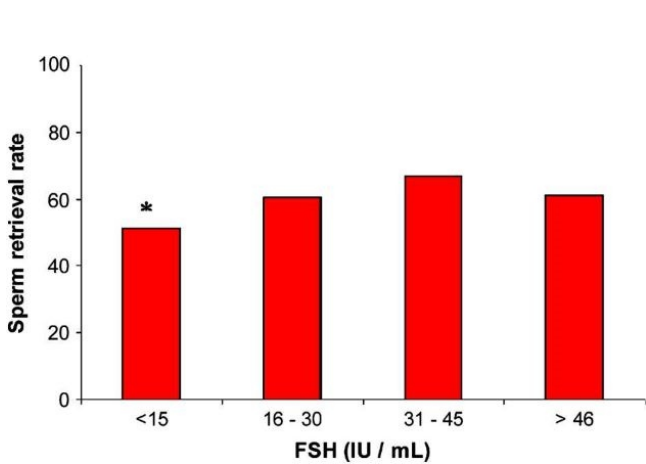


Figure 1

	Serum FSH (IU/mL)			
	<15	15-30	31-45	>45
n	245	360	124	63
Male age (yrs)	34 ± 7	36 ± 7	38 ± 7	37 ± 9
Female age (yrs)	31 ± 5	32 ± 5	32 ± 5	33 ± 6
Mean FSH (IU/mL)	9.0 ± 4.1	21.9 ± 4.0	36.5 ± 4.0	63.5 ± 22.8
Avg. vol. of larger testis	12 ± 5	9 ± 4	7 ± 4	6 ± 5
Histopathology (n)	127	314	102	58
Sertoli cell only (%)	34%	61%	68%	50%
Maturation arrest (%)	38%	16%	16%	28%
Hypospermatogenesis (%)	28%	23%	16%	22%

Study 2

The Value of Serum Follicle-Stimulating Hormone in Predicting Successful Surgical Sperm Retrieval in Cases of Male Infertility

micro-dissection testicular sperm extraction.

Objective:

To evaluate if the preoperative FSH levels are predictive of subsequent successful sperm collection SSC (Testicular sperm extraction TESE, microTESE, TESA) in cases of azoospermia prior to ICSI.

Method:

Eighty five (85) articles were identified and screened by title and abstracts, thirty five articles fit the study criteria were included in the final analysis.

Outcome measure:

Primary outcome measures were to determine if FSH is predictive of successful surgical sperm collection and to determine cut off value.

Secondary outcome measure was to determine whether different SSC methods have different cut off FSH values and if there is a correlation between FSH and clinical pregnancy rates or live birth rates following ICSI.

Ten out of the 35 studies gave cut off FSH values predicting SSC success. These ranged from <8.5 to <25.0 IU/L, with a mean value of 14.0 IU/L. The results suggested lower FSH levels are associated with increased SSR success.

Huang et al's prospective single centre analysis, studied 305 NOA males, TESE revealed that FSH was significantly lower in successful SSC (P <0.001) Mean FSH level : 11.05 Uiu/ul , sensitivity 83.5%; specificity : 74.5%

Huang et al , noted that genetic anomalies such as Klinefelters syndrome and Y chromosome microdeletions were in the exclusion criteria for 10 of the studies despite been established causes of azoospermia.

He seemed to think that the lack of homogeneity in the exclusion criteria's of the studies may have increased the risk of cofounders .

However one thing is clear, that there was an association between lower serum FSH levels and increasingly successful SSC.

The authors however, did not identify a discriminate FSH level to accurately predict SSC outcomes.

Conclusion

High pre-treatment FSH may predict poor surgical sperm collection rates, but does not necessarily preclude it.

TESE affords single or multiple random biopsies along testicular loci may fail to identify loci with adequate spermatogenesis to obtain sufficient sperm for ICSI.

Serum FSH alone may be misleading, apart from Sertoli cell only histological subtype of azoospermia, preservation of some Sertoli and germ cell function could maintain some negative feedback to the pituitary gland in some NOA males with normal FSH, LH and prolactin levels.

Different areas of the testes can have different histologies and a single biopsy or multiple random biopsies might miss areas of spermatogenesis and may not be representative of the most advanced histology.

Therefore it becomes imperative that clinicians must interpret results of endocrine function in azoospermic males with caution especially as it involves the decision for testicular exploration.

Recommendation

In Non Obstructive Azoospermic males with High pre-treatment FSH, Micro TESE analyses the testes through looking for the most advanced stage of spermatogenesis and represents the gold standard.

We opine that FSH alone may not be reflective of spermatogenesis and as such further research is needed to identify other biomarkers to refine decision making in the management of Non obstructive azoospermia.

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