

Correlation of Serum FSH and Rate of Testicular Sperm Retrieval in Non-Obstructive Azoospermia

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Abstract

Background: Sperm retrieval from men with azoospermia has evolved in recent times, providing patient hope for fulfilling their dream of having their own genetic child through testicular sperm extraction followed by intracytoplasmic sperm injection (TESE-ICSI). In the present study, we are correlating the serum follicle stimulating hormone (FSH) levels and the rate of testicular sperm retrieval. **Aim:** To correlate the serum FSH levels with surgically retrieved sperms from testes in non-obstructive azoospermia. **Method:** Sixty-six men presenting with male infertility, diagnosed with non-obstructive azoospermia based on standard guidelines were included in the study. The surgically retrieved tissue was washed in 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) gamete buffer media and scanned under an inverted microscope at $\times 400$. Outcome analysis was assessed through sperm retrieval rate. **Result:** Testicular sperms were successfully retrieved in 62% (41/66) of men. Sperm retrieval rate (SRR) with FSH values (Group A <10 , Group B $10-20$ and Group C >20) mIU/mL were 84% (26/31), 75% (12/16) and 15% (3/19), respectively. **Conclusion:** Chances of sperm retrieval in non-obstructive azoospermia using surgically retrieved sperm are as common for men with FSH levels <10 mIU/mL with 84% (26/31) retrieval as for the borderline $10-20$ mIU/mL FSH levels with 75% (12/16) retrieval. We do have retrieved sperms with >20 IU/mL serum FSH also which is not a contradiction for TESE for such patients; however, such patient's need to be counselled about the chances of successful sperm retrieval and the consequent pregnancy outcomes.

Keywords: Azoospermia, FSH, nonobstructive, retrieval, sperm

INTRODUCTION

Azoospermia is a medical condition of males having no sperm in the semen checked at least 4 weeks apart on two occasions. Azoospermia is diagnosed based on the absence of spermatozoa after centrifugation of complete semen specimens using microscopic analysis. Azoospermia may occur because of reproductive tract obstruction obstructive azoospermia (OA) or inadequate production of spermatozoa, such that spermatozoa do not appear in the ejaculate non-obstructive azoospermia (NOA). Non-obstructive azoospermia may be treated by defining the cause of low sperm production and initiating treatment. Genetic evaluation with Y-chromosome microdeletion analysis and karyotype testing provides prognostic information in these men.^[1]

The production of male gametes depends on the activity of two gonadotropins follicle stimulating hormone (FSH) and luteinising hormone (LH) on the testis. The work of LH is the building of testosterone by the Leydig cells. Since male germ

cell possess neither FSH nor androgen receptors, the action of FSH and testosterone occurs via Sertoli cells. Although the definite function of these two hormones is difficult to track, the evidence suggests that both FSH and testosterone are able to stimulate all phases of spermatogenesis. In males, FSH is required for the determination of Sertoli cell number and for initiation and continuation of normal sperm production.^[2]

Testicular sperm extraction (TESE) is a breakthrough in the treatment of male infertility. Especially for the patients diagnosed with non-obstructive azoospermia (NOA).

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However, unselected candidate NOA patients should be counselled, before undergoing surgical sperm retrieval, that only one out of seven men (13.4%) eventually fathers their genetically own child.^[3]

There are different ways to harvest sperms from a man with a blockage or nil sperm production in the ejaculate. The procedure for testicular sperm extraction can be divided as below:

Percutaneous epididymal sperm aspiration (PESA): A small needle is inserted through the skin of the scrotum to collect the sperms from the epididymis.

Microepididymal sperm aspiration (MESA): The sperm containing fluid is retrieved from the optimal area of the epididymis using high-power optical magnification.

Testicular sperm aspiration (TESA): In TESA, a needle is inserted in the testicle and tissue/sperm are aspirated.

Testicular sperm extraction (TESE): A small incision is done in the testis and the tubules are examined for the presence of sperms. This process is the optimal form to retrieve sperms from men with azoospermia.

Microsurgical testicular sperm extraction (micro-TESE): This procedure is performed for men with no sperm in the ejaculate and are azoospermic. A small incision is done in the scrotum through which both the testis can be seen and the sperms are harvested from them.

PESA and MESA are preferred choice for obstructive azoospermia patients and TESA, TESE, or micro-TESE is the preferred choice for non-obstructive azoospermia patients. In the present study, we are correlating the serum FSH levels and rate of testicular sperm retrieval in men diagnosed with non-obstructive azoospermia.

MATERIALS AND METHOD

This is a retrospective study conducted in our centre, New Delhi, north India, involving 66 azoospermia males who had surgical sperm retrieval between January 2020 and December 2020.

All the 66 subjects were diagnosed with non-obstructive azoospermia based on standard guidelines and were included in the study. All patients underwent a detailed physical examination, semen analysis was performed according to the World Health Organisation (WHO) criteria on at least two occasions, 4 weeks apart with high-speed centrifugation and the pellet was scanned for the presence of sperms and tests like fasting blood sugar, serum FSH, total testosterone, TSH and serum prolactin estimation were done.

In our study, testicular sperm extraction was performed for all the subjects under general anaesthesia between January 2020 and December 2020. The tissue was collected in a BD (Becton, Dickinson and Company) falcon center well dish containing V 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) plus gamete buffer media (GB) from Vitromed. The tissue was

washed thoroughly atleast three to four times in the GB media and the tubules were carefully teased with BD falcon 1 mL needle in fresh GB media. The media in which the tubules were teased is then collected in a small BD falcon 4 mL round bottom tube and allowed to settle for atleast 10–15 min before final scanning. The supernatant is transferred into a fresh round bottom tube and the specimen is then scanned under the inverted microscope at $\times 400$ for the presence of sperm in a scanning dish.

Ethical clearance statement

The study was approved by Independent Ethics Committee vide letter no. F.1/IEC/IFS/2023No.03 on 06/04/2023. Written informed consent was obtained for participation in the study and use of the patient data for research and educational purposes. The procedures follows the guidelines laid down in Declaration of Helsinki 2008.

RESULT

Total of 66 azoospermic patients were included in the study. The patients were divided into three groups based of serum FSH values: Group A (FSH <10 mIU/mL), Group B (FSH $10-20$ mIU/mL) and Group C (FSH >20 mIU/mL), respectively. Testicular sperm retrieval was successful in 62% of men (41/66). The sperm retrieval rate (SRR) among various groups are Group A (<10 mIU/mL): 84% (26/31), Group B ($10-20$ mIU/mL): 75% (12/16) and Group C (>20 mIU/mL): 22% (4/18), respectively [Table 1]. In all patients, total testosterone, TSH and serum prolactin were in the normal range.

The SRR was similar between Group A and Group B with no significant difference found between them ($P > 0.00001$). The SRR between Group B and Group C and between Group A and Group C showed a significant difference ($P < 0.00001$).

DISCUSSION

By the commencement of sperm retrieval techniques and assisted reproduction, especially the intracytoplasmic sperm injection (ICSI), has remarkably changed the perspective of azoospermia patients. ICSI has opened new hope for achieving pregnancy with sperm retrieved from the epididymes or testis. Satisfactory results have been achieved in various studies using these techniques for patients diagnosed with azoospermia.^[4]

Patients are unwilling to use the donor sperm as it does not give them their genetically own children, then the surgical sperm retrieval gives them a chance to father biological children.

Table 1: Percentage of sperm retrieval rate on the basis of serum FSH levels

Groups according to FSH range (mIU/mL)	Mean Serum FSH levels (mIU/mL)	Sperm retrieval rate
Group A (<10)	4.28	84% (26/31)
Group B ($10-20$)	14.47	75% (12/16)
Group C (>20)	40.28	22% (4/18)

Over the years, various methods of epididymal and testicular sperm retrieval have been reported to be used in conjunction with ART for men with azoospermia. Sperm retrieval techniques for obstructive azoospermia include microscopic epididymal sperm aspirations (MESA), percutaneous epididymal sperm aspiration (PESA), whereas testicular sperm aspiration (TESA) and testicular sperm extraction (TESE or micro-TESE) are the procedures of choice in non-obstructive azoospermia patients for sperm retrieval. With the introduction of these sperm retrieval techniques, the approach to managing azoospermic patients has changed significantly.^[5]

Our study is one of the few studies done in north India, in which we tried to correlate the serum FSH levels and rate of testicular sperm retrieval for patients diagnosed with azoospermia.

Azoospermia usually needs to encounter a more invasive procedure that is surgical sperm retrieval, to enhance their chances of sperm retrieval. The relationship of FSH with spermatogenesis is not straightforward in men with azoospermia. Therefore, elucidation of their actual prognosis is important to make the best decision concerning their treatment.^[6] Isolated FSH elevation is usually indicative of severe germ cell epithelium damage. Highly elevated FSH and LH levels, when associated with low-normal or below-normal testosterone levels, suggest diffuse testicular failure and may have either a congenital (e.g., Klinefelter syndrome) or acquired cause.^[7] Sperm retrieval rates reported earlier in the literature were inconsistent.^[8-11] According to Dabaja *et al.* spermatozoa are successfully retrieved in 50% of men with NOA. Other studies like Friedler *et al.*^[12] found an SRR of 40.6% in the NOA group consisting of 123 patients.^[12] A retrospective cohort study was done on 714 NOA patients conducted by Vloeberghs *et al.*^[3] reported successful sperm retrieval in 40.5% azoospermic patients and Cissen *et al.*^[13] reported successful sperm retrieval in 43.7% of NOA cases, respectively.

In our study, we correlated serum FSH levels as factors affecting sperm retrieval in patients with non-obstructive azoospermia. On subgroup analysis, on the basis of serum FSH levels, we have not found a correlation between FSH levels and successful sperm retrieval. Consistent with our results, a retrospective cohort study by Cissen *et al.*^[13] including data from 1371 TESE procedures found that lower levels of FSH were predictive of successful sperm retrieval. Another retrospective study done by Friedler *et al.*^[12] following testicular sperm retrieval on 123 patients failed to find a correlation of FSH levels to predict the presence or absence of testicular sperm after TESE. A prospective cohort analysis done by Saccà *et al.* on 63 NOA patients with conventional testicular sperm extraction found a sperm retrieval rate of 47.6%, he also could not find any statistical difference between the mean FSH levels and rate of sperm retrieval.^[14]

In conclusion, the present study was a comparative analysis of the FSH and SRR of surgically retrieved sperms in cases of azoospermia. The only limitations of our study were the small sample size and retrospective nature. Though it is well known that the sperm retrieval rate is low in non-obstructive azoospermia as compared with obstructive azoospermia, this still gives NOA men

to parent their genetically own child through surgically retrieved sperms. The NOA patient should definitely be counselled about the low success rate also. Since we have compared the sperm retrieval with serum FSH levels <10 mIU/mL to as high as >50 mIU/mL, and do find sperms in high FSH cases too, according to the present study serum FSH levels do not bear a definite role in the correlation with SRR so it is difficult to exclude the patient even if the FSH levels is >50 mIU/mL, despite of low sperm retrieval chances. In the end, we conclude that the serum FSH levels do not bear a definite role in excluding patients from undergoing procedures like testicular biopsy, which may eventually help them to become the genetic father of their child. The study definitely concludes that the higher the serum FSH levels lower the chances of retrieving sperms in the biopsy as we have found in FSH >20 mIU/mL, which is definitely a poor prognosis for such patients.

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Conflicts of interest

There are no conflicts of interest.

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