IOSR Journal of Nursing and Health Science (IOSR-JNHS)
e- ISSN: 2320–1959.p- ISSN: 2320–1940 Volume 7, Issue 2 Ver. IX (Mar-Apr .2018), PP 32-36
www.iosrjournals.org

Male Fertility Hormones and Testicular Doppler in Categorization of Azoospermia

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Introduction*: Azoospermia represents about 1% - 1.5% of male fertility factor of infertile couples. A male factor is solely represents about 20% - 30% of infertile couples.*
Objective*: To determine the role of Color Doppler Ultra-Sonography and measurement of testicular artery Resistive Index (RI) values in two groups, normospermic and azoospermic with male fertility hormonal results and correlates the RI values as predictive tool in categorization of azoospermia.*
Materials and Methods*: The study comprises (80) total subjects, (40) with normal sperm count (Normospermic) and (40) with (zero) pathological (azoospermic) subjects with their fertility hormonal (FSH, LH, Prolactine and Testosterone) results.*
Doppler performed by Chison QBit9 with high multi-frequency flat linear transducer D7L40L, testicular echogenicity, texture, volume, colour perfusion & testicular artery RI values from two groups (normospermic and azoospermic/with hormones) were studied and data was analyzed statistically by ***SPSS*** *software.*
Results*: Recent normospermic studies showed mean normospermic RI of 0.5 by Jeeet al., mean normospermic Resistive Index of ≥0.5 by Atilla et al & Biagiottiet al. and present studies showed mean normospermic Resistive Index of 0.54 and our study in (40) normospermic subjects testicular artery sampling showed waveform with a high flow in diastole, low downstream vessel impedance with mean (low) Resistive Index both testes (0.57±0.085) however, (40) azoospermic subjects with hormonal results showed waveforms with a little diastole flow, or reversed flow with mean Resistive Index both testes (0.61±0.14). Azoospermic subjects with normal FSH and LH showed mean Resistive Index both testes (0.58±0.125) and subjects with high FSH and LH values showed mean (high) Resistive Index value both testes (0.64±0.110).*
Conclusion*: Azoospermic subjects with normal FSH and LH hormonal results have RI value (0.58±0.125) closer or equal to mean normospermic RI (0.57±0.085) and this can be applied to obstructive azoospermia, however subjects with high FSH and LH values have RI values (0.64±0.123) closer or equal to mean azoospermic RI (0.62±0.146) and this can be applied to non-obstructive azoospermia. Further studies on large data sample were recommended.*
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Keywords*: RI, CD, US, PSV, OA, NOA, FSH, LH, Prolactine, Testosterone.*

Date of Submission: 09-04-2018 Date of acceptance: 23-04-2018

I. Introduction

The testicles were supplied from the internal spermatic arteries through the spermatic cord to the testis and they anastomose with the deferential and cremasteric arteries, testicular artery branches at the poster superior aspect of the testis, the point at which capsular arteries perforate the tunica albuginea and form the centripetal arteries that enter the testicular parenchyma. The testis requires a

stable blood supply for its function and maturation. Blood flow is the total amount of blood moving past a certain point, and is affected by two factors when flowing through a vessel, i.e. pressure and resistance, expressed as: flow pressure/resistance.

Azoospermia affects approximately 1% to 1.5% of the male population from 20% to 30% of men seek fertility workup, testicular biopsy reveals that those men have Sertoli cell-only pattern, maturation arrest, or hypospermatogenesis (1) Until recently, it was assumed that men with non-obstructive azoospermia were untreatable; indeed, those patients were often referred to as being sterile or having testicular failure, the only way those partners could have a child through donor spermatozoa or to adaptation, in addition it was previously thought that sperm must traverse the male reproductive tract before acquiring the ability to normally fertilize an egg. The success of treatment of men with obstructive azoospermia using sperm extracted from the epididymis or testis has changed this view, although testicular sperm have dramatically lower motility than those that have transmitted the male reproductive tract, those sperms can be used for intracytoplasmic sperm injection during in vitro fertilization, such observations led investigators to perform testicular sperm extraction with intracytoplasmic sperm injection for men with non-obstructive azoospermia, low pregnancy rates of 20% to 21% per attempt have been reported (2).

II. Patients and methods

Study comprises (40) normospermic group and (40) azoospermic group testes with their fertility hormones results (normal and abnormal) aged 21 to 48 years, studied by an andrologist and diagnosed of having pathological sperm count zero and they were sampled for male fertility hormones on the same day of ultrasound examinations, after explaining the study design written informed consent was obtained from all patients. Patients included in the study their major complaint was primary infertility, due to azoospermia after 01-24 months of unprotected sexual intercourse. Each patient had a complete semen analysis according to the WHO guidelines using semen samples obtained after 2 to 5 days of sexual abstinence, all patients referred by an andrologist were assessed by a medical history hernia, ambiguous genitalia, lifestyle habits such as nicotine or drug abuse, epididymitis, epididymal cyst, testicular mass, orchitis, trauma, torsion, Congenital absence of vasa differentia, hydrocele, spermatocele and varicocele were excluded from the study.

The serum total FSH, LH, Testosterone and Prolactine were examined on the same day of ultrasonography.

Scrotal ultrasound and colour Doppler were undertaken in a warm room with patient supine, scrotum supported by a towel placed between the thighs & penis resting on the abdomen, large amount of warm ultrasonic gel was used to minimize pressure on the scrotal skin, study of the spermatic cord is an important part of the examination, so as to exclude physically missed varicocele and suspected testicular torsion subjects. Each testicle was measured in three dimensions and the volume calculated automatically by the machine. Doppler flow was measured in each testis using a trans-scrotal approach with a 14 - MHz linear array probe (Chison GBit9, China, D7L40L linear transducer). The PSV and EDV were calculated by the machine, recorded bilaterally for each patient, perfusion was categorized as studied by University of Padova (3) (Cat. 0, 1 & 2) The RI was then calculated on each testicle at an intratesticular artery (transmediastinal). At least two Doppler waveforms had to be obtained from the artery and PSV was also recorded. RI values were calculated in both groups and statistically analyzed by SPSS.

III. Results

(40) Normospermic showed Rt testicle RI 0.59±0.09 with significant 2-tailed paired sample correlation P value (0.001) and Lt testicle RI was 0.55±0.08 on Lt side testicle with significant 2-tailed paired sample correlation P value (0.000) with mean RI both testes: 0.57±0.085.

(40) Azoospermic with hormonal results showed 0.61±0.14 means RI both testes. With normal FSH hormone level the Rt. RI was 0.58±0.11 with significant P value (0.025) and Lt. RI was 0.58±0.14 with significant P value (0.031) with mean RI both testes = 0.58±0.125. with abnormal FSH hormone level the Rt. RI was 0.64±0.04 with significant P value (0.033) and Lt. RI was 0.64±0.15 with significant P value (0.035) with mean RI both testes = 0.64±0.95. (3) normal LH hormone level the

Rt. RI was 0.59±0.13 with significant P value (0.024) and Lt. RI was 0.59±0.13 with significant P value (0.031) with mean RI both testes = 0.58±0.115.!4) abnormal LH hormone level the Rt. RI was 0.65±0.14 with significant P value (0.029) and Lt. RI was 0.62±0.16 with significant P value (0.034) with mean RI both testes = 0.64±0.150.(5) normal Testosterone hormone level the Rt. RI was 0.62±0.14 with significant P value (0.030) and Lt. RI was 0.63±0.14 with significant P value (0.029 with mean RI both testes = 0.63±0.140.(6) abnormal Testosterone hormone level the Rt. RI was 0.60±0.10 with significant P value (0.026) and Lt. RI was 0.58±0.15 with significant P value (0.039) with mean RI both testes = 0.59±0.125.(7) normal Prolactine hormone level the Rt. RI was 0.62±0.11 with significant P value (0.025) and Lt. RI was 0.59±0.14 with significant P value (0.030) with mean RI both testes = 0.61±0.140.(8) abnormal Prolactine hormone level the Rt. RI was 0.60±0.14 with significant P value (0.033) and Lt. RI was 0.62±0.16 with significant P value (0.037) with mean RI both testes = 0.61±0.150.

IV. Discussions

Ezeh UIO, Moore HDM, Cooke ID (4) Study showed PSV and RI can be used as a predictor for testicular function with significant P value (0.001 & 0.001) respectively. Our study in normospermic (40) subjects showed positive RI values correlations with testicular artery PSV with significant 2-tailed paired sample correlation P value (0.000 & 0.003) Rt. & Lt. testes respectively.

Study of Biagiotti (5): Showed that normospermic RI ≥0.50, study of Pinggera (6) showed that normospermic RI = 0.54 and RI >0.60 with P value (0.001) found in oligospermia patients.

Our study in (40) normospermic subjects: Showed high flow in diastole, low downstream vessel impedance with Rt testicle RI of 0.59±0.09 with significant 2-tailed paired sample correlation P value (0.001) and Lt. testicle RI of 0.55±0.08 with significant 2-tailed paired sample correlation P value (0.000) with mean RI both testes of 0.57±0.085.

Kupat Holim Mehuhedet Unit, Shaare Zedek Medical Center, Jerusalem (7) study showed that testicular volume cannot predicts presence or absence of sperms.

Our study in normospermic (40) subjects RI values showed positive correlations with testicular volume without significant P value but showed mean normospermic volume of 15.00±2.6cc with highly significant correlation P value (0.000).

Joel H. Hillelsohn, MD (8) study showed that with oligoasthenozoospermia RI >0.60 with significant P value (0.001). Departments of Urology and Radiology II, Medical University Innsbruck, Austria Accepted for publication 10 August 2007 (9) suggest that: RI of greater than 0.60 might be pathological and the intratesticular RI as measured by CDUS seems to be a reliable indicator for routine clinical use to identify sub fertile men.

Doppler indices have been obtained about blood flow and vascular impedance that cannot be obtained from velocity information alone. These indices depend upon the volume, perfusion categorizations (3) measurements of PSV and RI values. Medical University Innsbruck, Austria stated that the measured serum concentration of total and free testosterone, LH, FSH or Prolactine was within normal values, with no significant difference in the hormonal profiles of infertile men, with or with no pathological spermiograms (4) The widely used index was the RI for the measurement of transmediastinal blood flow, the RI has been used to date in both animals and humans. Gumbsch et al (10) used colour-coded duplex US to examine the testes of 42 dogs which were normal on clinical examination, and defined normative values of testicular blood flow using RI. Therefore, the present results might be applicable to males in or after puberty. In the present study there was a significantly greater RI (RI>0.60 P <0.001) in patients with oligoasthenozoospermia and Joel H. Hillelsohn, MD (8) and this finding supports the use of testicular spectral Doppler sonography as a noninvasive tool for evaluation of testicular function is associated with impaired spermatogenesis. Battaglia et al (11) reported that in 16 normozoospermic patients there was a significantly greater testicular volume, lower PI in an intratesticular artery and higher seminal plasma nitrite/nitrate concentrations than in 40 men with oligo or azoospermia. There is currently no published explanation for the significant positive relationship between RI and sperm count/ spermatogenesis.

Testicular arteries are target organs for androgens, and in infertile men testicular arteries have a narrow lumen caused by enlarged endothelial cells, a thickened sub endothelial layer and an abundant adventitia rich in connective tissue fibers and ground substance, as reported by Reproductive

Medicine Unite, Societal Latina Study di Medicina Della Riproduzione (S.I.S.ME.R) Bologna , Italy (12) RI and PSV proved to be a reliable tool to be routinely used in the clinical study of infertile/dyspermic males, whereas EDV FSH and testicle volume did not, in our study we have correlate the relationship between RI values of 30 subjects with their hormonal profile done by different methods,

Joel H. Hillelsohn, MD (8) study showed that with oligoasthenozoospermia RI >0.60 with significant P value (0.001). Departments of Urology and Radiology II, Medical University Innsbruck, Austria Accepted for publication 10 August 2007 (13) suggest that: RI of greater than 0.60 might be pathological and the intratesticular RI as measured by CDUS seems to be a reliable indicator for routine clinical use to identify sub fertile men. International Urology and Nephrology (14): The study showed no correlations were found between serum LH and testosterone levels and testicular volumes. Cavallini, via Mascheraio 46, 44100 Ferrara, Italy. Volume 90, Issue 9 December 2002 Pages 903–908 (15): Conclusions the RI and PSV are reliable indicators for routine clinical use to identify infertile/dyspermic men, while EDV, FSH and testicular volume are not. The RI and especially PSV clearly differentiated obstructive from unconstructive azoospermia.

Our study correlates the relationship between male fertility hormones values of 40 subjects with testicular, volume, testicular perfusion as categorized by Padova University, Peak Systolic Velocities and resistivity index were calculated by the machine and concludes that:

Testicular volumes and PSV showed low with normal FSH, LH & Testosterone hormones and showed high with abnormal FSH, LH & Testosterone hormones, except with Prolactine the relation with different and showed high volume & PSV with normal and low volume & PSV with abnormal levels.

RI values showed normal values with normal FSH & LH and high values with abnormal FSH & LH hormonal levels.

RI values showed rather high values with normal Testosterone & Prolactine and low values with abnormal Testosterone & Prolactine hormonal levels.

RI values showed negative correlations with testicular volume with no significant 2-tailed paired sample correlation P value

RI values showed positive correlations with testicular artery PSV with significant 2-tailed paired sample correlation P value (0.024) Lt. Testicle only.

Our study in(40) Azoospermic with hormonal results showed: Rt. RI 0.61±0.132 & Lt. RI. 0.61±0.151 with significant 2-tailed paired sample correlation P value 0.000.

RI values were significantly different in normal and abnormal hormones: Azoospermic with (normal FSH & LH) have mean RI (0.58±0.120). Azoospermic with (abnormal FSH & LH) have mean RI (0.64±0.123). Azoospermic with (normal Testosterone & Prolactine) have mean RI (0.62±0.140). Azoospermic with (abnormal Testosterone & Prolactine) have mean RI (0.60±0.138).

Sussman EM, Chudnovsky A, Niederberger CS. Hormonal evaluation of the infertile male: has it evolved. Urol Clin North Am. 2008; 35 (16):147, vii–55: Their study concludes that: Normal levels of LH and FSH are expected in OA; however, LH and FSH can be low or elevated in NOA.

Our study agree with their findings and confirmed that: azoospermic subjects with normal FSH and LH hormonal results have an RI values (0.58±0.125) equal or similar to those are normospermic (0.57±0.085) and subjects with high FSH and LH values (0.64±0.095) were found have higher RI values or similar to those are azoospermic (0.62±0.146).

V. Conclusions & Recommendations

Our study concludes that: azoospermic group with normal FSH and LH hormonal results have low Resistive Index values (0.58±0.125) equal or similar to those are normospermic (0.57±0.085) and this can be recommended as reference RI value for obstructive azoospermia, however azoospermic group with high FSH and LH values have higher Resistive Index values RI (0.64±0.123) equal or similar to those are azoospermic (0.62±0.146) and this can be recommended as reference RI value for non-obstructive azoospermia, further studies on large data sample azoospermia with male fertility hormonal results were recommended.

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Mohammed K. Magzoub "Male Fertility Hormones and Testicular Doppler in Categorization of Azoospermia"." IOSR Journal of Nursing and Health Science (IOSR-JNHS) , vol. 7, no.2 , 2018, pp. 32-36.