Review Article

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Assessment of Male Reproductive Health: Obesity, Sperm DNA Fragmentation, Yq micodeletion, Endocrinal Profile

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Abstract

The main aim of our study is to highlight the few important aspects of male reproductive health and thus male infertility. The male infertility is a common issue among couples these days. Various infertility clinics and hospitals have developed to solve this problem however, specialists are not evaluating much after semenogram when it comes normal whereas only half of the problem is recognized by semenogram. So, the question should be what next to evaluate after that: Endocrinal profile, body mass index, karyotype, chromosome microdeletion, sperm DNA fragmentation index of patient? If we as clinicians bypass these tests, we might miss the underlying disorder or inadvertently transfer it to the offspring. Moreover, it also affects the outcome of various techniques of assisted reproduction.

Keywords: Sperm DNA fragmentation; Ychromosome microdeletion; Male reproductive health.

Introduction

Male reproductive health is important to evaluate fertility. Half of fertility problems are basically related with male reproduction. Either external or internal, genetic or nongenetic causes should be evaluated. More than 50% of infertility problems of male areexplained by semanogram. Next to be evaluated for male reproductive health; either endocrinology profile, or genetic tests; Karyotyping, yqmicrodeletion, Sperm DNA fragmentation or both. Some note worthy issues which are really related to and need to discuss for male reproductive health

Obesity and male reproductive health

Male obesity is related with reduced blastocyst development, reduced fertilization rate. That's why outcome in couples undergoing ART is poor when males have high BMI. (Bakos et al. 2010, Hwang et al. 2011). Increase BMI influences hypothalamo-pituitary axis (HPA) which is because of decrease sex hormone binding globin and testosterone and increases Estrogen.

In obese male, sperm quality is reduced because of molecular changes like epigenetic modifications to the sperm through changes to noncoding RNA content, acetylation and methylation (Youngson et al. 2011, Daxinger et al., 2012). Studies suggested that proteomic profile of patient has also changed in obese than nonobese. Normally, methylation of DNA of sperm is required for the normal process of spermatogenesis and productive pregnancy. Hypermethylation and hypomethylation both significantly affect the sperm production. Altered level of methylation in promotor region of MTHFR gene are associated with decreased sperm function.

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Endocrinal profile and male reproductive health

Male infertility due to decreased spermatogenesis may result from hypothalamic, pituitary and testicular pathology. Approximately 20% of male infertility results from endocrinopathies. Testosterone (TH) is a vital sex hormone playing role in male fertility. Other are Follicle stimulating hormone (FSH), Luteinizing hormone (LH), prolactin and inhibin. These need to be evaluated first. In addition to that thyroid profile should also be evaluated.

Many cases of infertility do not have significant medical history. Like diabetes mellitus can cause erectile disfunction and ejaculatory disfunction. In view of systemic analysis, anosmia suggests hypothalamic etiology (Kallmann's syndrome) or pituitary etiology. Young syndrome is a form of obstructive etiology and Kartangener's syndromeis a form of ciliary defect. These present as infertility along with respiratory bronchiectasis and sinusitis. Galactorrhoea and headache.

Sperm DNA fragmentation and male reproductive health

Male reproductive health as well as fertility is determined by the quality of spermatozoa. Damaged sperm DNA has well-known role in reduced fertilization rates, embryo quality, and, pregnancy rates, higher rate of spontaneous abortion (Lewis SEM, 2013, Simon et al. 2013). In the process of spermatogenesis, histone replaced by important transitional protein, protamine plays a role in compaction of chromatin. This protamine is a basic core protein in the head of spermatozoa. The content of protamine is indispensable for the final phase maturation of spermatozoa nucleus.Four important method of estimation of sperm DNA fragmentation, DNA fragmentation index (DFI) can be assessed by Sperm chromatin structure assay (SCSA), TUNEL assay (TdT-mediated –dUTP nick end labelling), COMET assay (single gel electrophoresis) and AOT (acridine Orange staining technique). Sperm chromatin structure assay is a gold standard method for DFI estimation. This test is based on flow cytometry. The newer and economical technique is sperm chromatin dispersion test (SCD). This assay is based on the principle that sperm with fragmented DNA fails to produce characteristic halo of dispersion that is observed in sperms with nonfragmented DNA following acid denaturation. In our observation DFI of normozoospermia in fertility patients may have high DFI and oligozoospermic infertility patient have even higher DFI.

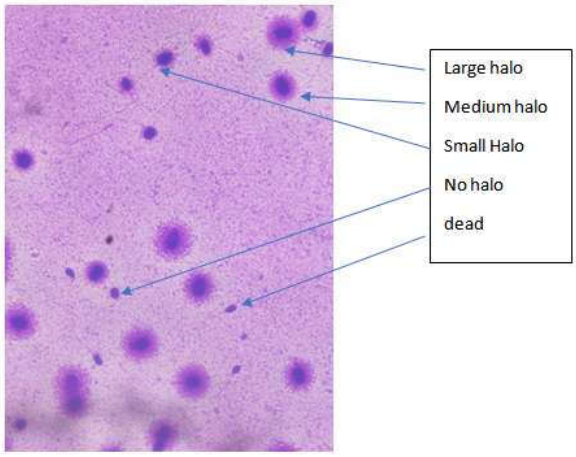

Fig. 1: SCD method showing processed sample of normozoospermic man

Varicocele and male reproductive health

Overall distribution of varicocele in cases of male infertility is 37% (Poongothai et al. 2009). What is the mechanism of infertility in this is not clearly understood? Redmon et al. (2002) kept varicocele in systemic basis for male infertility. He hypothesized that varicocele may not have any association or effect on infertility. Several researchers reported that varicocele is related with genetic factor. Sun et al. 1999, reported gene changes occurred in the form of point mutation in USP9Y genes. Some commonly reported deletions of various STS markers expressed in Y-chromosome in varicocele cases that were sY153, sY158, sY254 and CDY1 gene (Rao et al. 2004). All these outcomes to 1–55% frequencies of genes deletions and point mutation in varicocele cases of infertility.

Karyotype

Frequency of chromosomal abnormality ranged from 2–8% in unselected infertilemen (Ferline et al. 2006). These are increased to 5–7% in oligozoospermic and 10–15% in azoospermic male. Balanced autosomal translocations are more frequent in infertile men. Reciprocal translocations involving X chromosome were more common than Y chromosome, in later if break point confines to euchromatic region results in infertility. This

cytogenetic evaluation of unselected infertile males are very vital.

Ychromosome microdeletion and Male reproductive health

All genes related to male reproductive health are mainly located on Ychromosome. It has two arms; short p and long q. both have telomeric ends and PAR regions. This Ychromosome is loaded with palindromic sequences in p arm. Most of them are deleted in infertile men. These sequences are present in azoospermia factor region (AZF region). These AZF regions are classified into AZFa, AZFb, AZFc and AZFd. Deletion events are common in Ychromosome because of its structural organization. According to European academy of andrology (EAA) firstly, six sequence tagged sites(STS) are evaluated to detect deletion. Overall prevalence of this deletion in Indian population is approximately 8% (Krasuz 2013). Yq microdeletion has association with reduced sperm DNA integrity (Perrin et al. 2013, Rouen E, 2013 Shamsi 2012).

AZFa deletion affects germ cell level; as a result, spermatogonia or spermatocytes are not formed and patient presents with azoospermia. AZFb deletion may also affect germ cell level; similarly, spermatogonia or spermatocytes may or may not form. Patient presents with oligozoospermia or azoospermia. AZFc deletion affects late stages of spermatogenesis, therefore, spermatocytes and spermatids are formed. Patient presents with oligozoospermia or normozoospermia but he may also develop oligozoospermia or azoospermia.

Conclusion

Accurate and comprehensive examination of male reproductive health in terms of BMI, harmonal profile, sperm DNA fragmentation index, varicocele status, Karyotype profile, and Yq microdeletion status in combination with conventional semenogram could play a significant instructive role for prevention or correction of the underlying pathology in prior ART planning. Author insists the prerequisite of genetic evaluation of infertile couples especially male partners to prevent potential psychological trauma to couples after failure of ART ortransferring defect tothe offspring.

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