Male Infertility: Whom to treat – person or his sperm

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Infertility per se is a unique condition to the physicians as it itself is not a disease state. Infertility may be caused by some disease or it may prevail in perfectly healthy couple. Primarily it is a social problem followed by psychological and medical disorder. While 85% of couples are able to conceive after one year of unprotected intercourse, approximately 15% of couples are unable to initiate a pregnancy without some form of assistance or therapy. These patients are said to be "primarily infertile." In approximately one-third of these couples, a male factor appears to be singularly responsible, and in an additional 20% both a male and a female factor can be identified. Therefore, a male factor is at least partly responsible for difficulties in conception in roughly 50% of these couples.

In treating male factor infertility, the treatment is not precisely concerned about the health of the individual but about the health of his gametes. The end result of infertility treatment is to achieve a pregnancy and to get a viable delivery. Though the production of gametes is a natural phenomenon but under certain circumstances it needs pharmacological help. This is particularly useful for female gametes but for male gametes the situation is difficult. It is to be kept in mind that during ovulation a secondary oocyte is released which is a diploid cell but in case of male the released spermatozoon in the ejaculate is a haploid cell. Hence it is difficult to influence the production and to maintain quality control of male gametes in vivo.

In the light of above factors it is useful to analyse critically how male or seminal factor disorder is diagnosed. It is more important to consider the available therapeutic approaches carefully regarding their efficacy. It is always difficult to detect the etiology of seminopathy.

Approach to identify possible aetiological factors

Key processes in male reproduction that can be disrupted may be classified as:

I. Hormonal Mechanisms
II. Mechanisms Controlling Spermatogenic Output
The hormonal mechanism may be disturbed either by hyper or hypo secretion of hormones or due to mutation of definite genes controlling their secretion. Rest of the mechanisms is usually affected by genetic or enzymatic disorder - which directly affects the spermatozoa.

In a study conducted by Dey et. al. it has been found that about 82% cases of male infertility are idiopathic and rest are hormonal defects. This is probably the general experience and every one will agree that conventional treatment of male infertility is very unrewarding. Selection of medical agents is almost always empirical.¹

The diagnostic procedures like semen analysis tell us about conditions like azoospermia, oligoasthenozoospermia, necrozoospermia etc. Sperm function tests indicate about ability of sperm to fertilize. Values of serum testosterone reflect Leydig cell function and provides an easy available indicator of intra testicular testosterone. Measurement of circulating LH and FSH levels allows the clinician to determine if a patient's endocrine dysfunction is the result of primary testicular failure or hypothalamic and/or pituitary deficiency. Though there are some cutoff values for seminal parameters but on many occasions the semen with lower values are surprisingly fertile. None of the above tests can pinpoint etiology or can give any direction of treatment.

Seminal plasma may contain some form of specific antigens which provoke production of iso or auto antibodies. These may result in sperm immobility or interfere with sperm-ovum interaction.

Immunological tests like MAR (Mixed Antigen Reaction) test or immunobead test can be performed in all cases of unexplained infertility. There are significant tests in assisted reproductive technologies but not performed at routine semen analysis. However Post
coital test or sperm cervical mucous contact test (SCMCT) though controversial may provide indirect evidence of either iso or autoimmune defect through sperm agglutination (head to head, tail to tail, or head to tail) when sperm wash and IUI may be of help.

Recently role of oxidative stress on sperm function and abnormal semen profile has been emphasized. Theoretically sperm function is impaired or reduced due to oxidative stress. Oxidative stress may develop due to improper balance between reactive oxygen species (ROS-Prooxidants) and scavenging activities of the endogenous antioxidants. Oxidative stress induces spermatozoal membrane and nuclear chromatin damage leading to immobility and death of spermatozoa. Prooxidants are generated by leucocytes, immature and defective spermatozoa, genital tract infection and varicoceole. Endogenous antioxidants are superoxide dismutase (SOD), catalase and probably glutathione peroxidase or reductase (Sikka et al). At present, no standardized oxidative stress level is known which may be considered to be normal because some amount of ROS is essential for proper spermatozoal function. ROS can be directly measured by luminometers. In a study conducted by Chattopadhyay et al at IRM Kolkata very high ROS levels were found in abnormal semen samples like astheno, pyospermia and OAT syndrome. On the other hand very low levels of ROS were observed in proven fertile men. Sometimes high ROS levels were also found in normal semen samples with unexplained infertility which may lead to fertilization failure. However no cutoff value of ROS level has been found so far which may be considered normal or abnormal. ²,³

**Genetic background of male infertility**

Recent publications have highlighted that genetic defect leading to male infertility can often be transmitted to the male offsprings. There are at least three types of nuclear DNA mutations that have some relations with spermatogenesis. Mutations have been found in sex chromosomes (X- the androgen receptor gene; Y- the AZF gene and in the autosome 7- the gene resulting in cystic fibrosis in the presence of congenital absence of vas or CAV). Mutations in the mitochondrial DNA have also been reported in sperm with reduced motility.

Further expansion of our knowledge about genetic factors leading to spermatogenetic failure is based on the fact that in approximately 3 – 8% of men with sperm counts less than 5 million/ml, there are significant deletions in the long arm of their Y chromosome. The results suggest that the larger the deletion, lesser is the chance of finding sperm at testicular retrieval especially if the deletion involves AZFa. A number of key genes have been identified for their involvement in the physiological control of spermatogenesis including maturation in the androgen receptor gene & the FSH & LH receptor genes. To date most of the specific gene defects causing infertility have arisen from identification of
Studies towards identification of a genetic cause of infertility have shown that some azoospermic men had small Y-chromosomes resulting from the loss of genetic material on the long arm of the Y chromosome (Yq) that led to look for Y chromosome deletions. For example with microdeletions in the long arm of the Y chromosome testicular histology may show Sertoli-cell only syndrome, germ cell arrest or hypospermatogenesis. To date, the generally held view is that about 3-8% of men with previously designated idiopathic seminiferous tubule failure with sperm counts less than 5 million /ml have a Y chromosome deletion. Numerous studies have now confirmed that these deletions are large & can affect two regions of the Y chromosome described as interval 5 & 6 & several genes, DAZ (deleted in azoospermi) & RBMY (RNA binding motif), both encoding RNA binding proteins, have been casually linked to defects in spermatogenesis. The DAZ gene clusters present in Y chromosome has an autosomal homologue DAZL (DAZ like) located on short arm of chromosome 3 (3p2q). both DAZ & DAZL are RNA binding proteins. De novo mutation in DAZL gene are associated with male infertility as reported by Thangaraj et al (in press). These genes are present as multiple copies &
deletions arise de novo by recombination events between long stretches of highly repetitive sequences which represent palindromes. Functional analyses of these deletions have established 3 azoospermia regions termed AZFa, AZFb & AZFc & there is general agreement that the larger deletions, involving AZFa & b, as well as AZFc, are associated with severe damage to spermatogenesis & usually indicated the absence of germ cells of any type from the testis. Deletions limited to AZFc are associated with severe oligozoospermia or azoospermia & if, the later is present, testicular sperm suitable for ICSI can often be found in testicular biopsies. The involvement of the AZFc region occurs in about 80% of the deletions. Similar data has been presented in a study in Indian population by Thangaraj et al 2003. Deletion in Y chromosome has been found to be in AZFc region in 82.8% cases followed by AZFb 55.2% and AZFa 24.1%. This fact has led to the need to determine whether a Y deletion exists in the routine evaluation of an infertile male with a sperm count of <5 million/ml as transmission of a Y deletion from father to son has been shown to occur by the use of ICSI.7,8.

There are multiple control points in the physiology of spermatogenesis that could be disrupted by mutations in specific genes. The resultant defects are divisible into two major groups, those that are testis specific & result in infertility as the only phenotype & others that involve alterations in many organ systems. Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations typically manifest in men with azoospermia due to CAV which occurs in 1%-2% of men presenting with infertility. It is anticipated that at least 2600 genes are required to function normally to result in the production of fertile sperm & clearly many of the defects resulting from mutations of these genes have not yet been defined. A variety of approaches have been undertaken to identify genetic defects causing infertility. This continuous search reveals the need for Sertoli cells to produce stem cell factor that acts, through its receptor c-kit on spermatogonia, to stimulate spermatogonial mitosis & survival. A mutation in the c-kit gene in families results in the condition of human piebaldism, due to failure of normal melanocyte migration, but did not result in infertility or anaemia.9-13

**Reasons for treating the gamete & not the individual in male infertility**

Since the availability of ART procedures the treatment at gamete level has become feasible. This therapeutic option has helped us to review the efficacy of conventional treatment and the usual diagnostic procedures. Since in male infertility, treatment of the individual is not very effective, treatment at the gamete level has always achieved considerable attention and importance. If we look at the evolution of treatment of male infertility it will be evident that the trend is towards gamete manipulation. During the era of Mahabharata “Niyog pratha” was in vogue whereby the female partners of azoospermic males used to have conception by natural intercourse with fertile men.
Artificial insemination with husband or donor semen became a procedure where crude semen was injected in the female vagina. Then came Intra Uterine Insemination (IUI) where isolated sperm were introduced in the uterine cavity after proper preparation. Now a days even precursor of sperm cells obtained by testicular sperm extraction or aspiration(TESE / TESA) containing genetic material can be injected in the cytoplasm of oocyte by the process called ICSI.

**Broad outline of diagnostic procedures**

While evaluating the diagnostic procedures and conventional treatment options and to compare them with ART procedures it is necessary to consider briefly the merits and demerits of available diagnostic and therapeutic procedures (Table I).

**TABLE I**

<table>
<thead>
<tr>
<th>Diagnostic Tests</th>
<th>Merits and demerits</th>
</tr>
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<tbody>
<tr>
<td>Semen Analysis</td>
<td>*Cornerstone of investigation of male factor infertility</td>
</tr>
<tr>
<td></td>
<td>*WHO 1992 standard is followed</td>
</tr>
<tr>
<td></td>
<td>*Normal semen sample does not require further investigations of the male</td>
</tr>
<tr>
<td></td>
<td>*Does not indicate functional capacity of sperm.</td>
</tr>
<tr>
<td>Physical Examination</td>
<td>*Performed in seminopathy to exclude any correctable defect like varicocele.</td>
</tr>
<tr>
<td></td>
<td>*Correction of varicocele has not proved useful in improving seminopathy</td>
</tr>
<tr>
<td>Sperm Function Tests</td>
<td>*Rough idea about fertilizability</td>
</tr>
<tr>
<td></td>
<td>*Not useful so far medical treatment is concerned</td>
</tr>
<tr>
<td>Sperm survival in vitro</td>
<td>*Useful for fixing up timing for IUI</td>
</tr>
<tr>
<td></td>
<td>*May differ from what happens in vivo</td>
</tr>
<tr>
<td>Post coital test</td>
<td>*Helpful if semen is not available by masturbation</td>
</tr>
<tr>
<td></td>
<td>*Sperm agglutination ? immunological defect</td>
</tr>
<tr>
<td></td>
<td>*Not of diagnostic value</td>
</tr>
</tbody>
</table>
Tests for oxidative stress (OS)  
*Can justify role of antioxidants  
*Results not yet standardized

CASA  
*Better idea about sperm motility  
*Very costly - not useful for day to day investigation.  
*Can be highly inaccurate in samples with very high or low concentration  
*Lack of understanding of specification & limits might interfere with result

Karyotype  
* In men with sperm count<5mill /ml  
*Mandatory in azoospermia seeking ICSI  
*Translocation or aneuploidy can cause defective spermatogenesis  
*Small Y chromosome - deletion5

**Therapeutic approach**

Conventional therapeutic approaches are as follows:

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>Benefits and limitations</th>
</tr>
</thead>
</table>
| Antioestrogens eg Clomiphene citrate | *Failed to prove any benefit in prospective randomized trial.  
  *Still commonest oral agent used  
  *Dose finding is difficult |
| Vitamin B complex & Vitamin E | *Initial improvement of motility  
  *No long term effect |
| Androgens               | *May improve motility  
  *Short term effect |
| Antioxidants            | *Oxidative stress may cause sperm defect |
* Further clinical trial necessary

Pituitary Gonadotrophins
*Useful in very small number of hypogonadotrophic hypogonadism cases
*Very expensive

IUI
*Not much useful in severe seminal defect
*Marginal increase in pregnancy rate in border line group reported.

<table>
<thead>
<tr>
<th>CLINICAL &amp; PATHOLOGICAL TYPES OF MALE INFERTILITY</th>
<th>FREQUENCY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreatable sterility</td>
<td>12%</td>
</tr>
<tr>
<td>Treatable conditions</td>
<td>18%</td>
</tr>
<tr>
<td>Untreatable subfertility</td>
<td>70%</td>
</tr>
<tr>
<td>Gonadotrophin deficiency</td>
<td>0.5%</td>
</tr>
<tr>
<td>Disorders of sexual function</td>
<td>0.5%</td>
</tr>
<tr>
<td>Oligozoospermia</td>
<td>35%</td>
</tr>
<tr>
<td>Asthenozoospermia and teratozoospermia</td>
<td>30%</td>
</tr>
<tr>
<td>Normozoospermia with functional defects</td>
<td>5%</td>
</tr>
<tr>
<td>Obstructive azoospermia</td>
<td>10%</td>
</tr>
<tr>
<td>Sperm autoimmunity</td>
<td>7%</td>
</tr>
<tr>
<td>Reversible toxin effects</td>
<td>0.02%</td>
</tr>
<tr>
<td>Primary seminiferous tubule failure</td>
<td>12%</td>
</tr>
</tbody>
</table>
**A MODEL STUDY:**

A study conducted at RFC, Kolkata showed different patterns of seminal defects and their treatment outcomes. Between January 2000 and October 2002, 1940 couples attended our clinic. Seminal pathology was detected in 646 of them (30%). They were treated with drugs mentioned below:

- Gonadotrophines (HMG/HCG), Clomiphene, Androgens, Bromocryptine,
  - L-Thyroxn, vitamins, proteins, Newer Drugs.

All these cases were reevaluated with an objective to confirm diagnosis, which involved repeat semen analysis after a period of 3 to 4 days abstinence, keeping a close watch on materials of semen collection jar to avoid contamination with toxic materials. Collection of semen should be smooth to avoid erroneous result. After seminopathy was confirmed the etiology was investigated. Semen analysis, sperm survival, sperm function tests, hormone estimations, biochemical evaluations starting from sugar, to basic tests of renal function were performed. Following complete evaluation only in 10-15% cases cause of seminopathy could be detected. The major bulk of 85-90% remained idiopathic. Depending on above findings treatment protocol was selected for particular patient. For patients with specific defects selection of treatment was not difficult. For hypogonadotrophic hypogonadism (low FSH and LH) hMG / hCG, Bromocryptine and L-Thyroxn for hyperprolactinaemia and hypothyroid respectively and different preparations of Testosterone for hypogonadism were indicated. For maturation arrest in spermatogenesis, gonadotrophine and androgens were also drugs of choice. For inflammatory and infective condition antibiotics, antioxidants and anti-inflammatory drugs were used.

Selection of treatment protocol for idiopathic group needed more expertise. The clinical presentations were oligozoospermia, asthenozoospermia, oligoasthenozoospermia and combination of them. For oligozoospermia the degree was found out. In severe group (<10 x 10^6/ml), partial obstruction were ruled out because this may be one of the commonest causes of this type of abnormality.

Sometimes for moderate (10-15 x 10^6/ml) and mild (15-20 x 10^6/ml) oligozoospermia support with vitamins, antioxidants and nutrients were of help. In all cases clomiphene was considered. Gonadotrophine alone or in combination were also useful but at the same time expensive as well. Asthenozoospermia presented real challenge to us. Severe asthenozoospermia was rarely found to improve with androgens and/or hCG. For mild
and moderate group vit – E, antioxidants & androgens were helpful. In this series treatment was selected according to above criteria.

For oligozoospermia combination of clomiphene with hCG, androgens with hCG, vitamins or clomiphene alone were considered. Idiopathic pyospermia might not respond to usual treatment. For all the above mentioned conditions sperm wash followed by Intra-Uterine Insemination (IUI) or assisted reproductive technologies were also considered.

For mild to moderate group of oligoasthenozoospermia semen wash, sperm preparation in suitable medium followed by IUI gave encouraging results. Motility of sperm was improved by washing and incubation in suitable medium (HAM F-10, EARLES) fortified with adjuvants. Pentoxifylline treatment of sperm in vitro has been noted to decrease sperm production of superoxide anion by 50%. Platelet-activating factor (PAF), lyso-PAF, and lysophosphatidyl choline have been shown to increase sperm motility and forward progression in vitro and have been postulated to act as ROS scavengers. Administration of antioxidants like L-carnitine and L-acetyl carnitine has been found to be effective in increasing sperm motility in patients affected with idiopathic asthenozoospermia. Antioxidant molecules such as glutathione and coenzyme Q10 were also reported to improve semen quality in infertile males.¹⁴

By centrifugation and concentration technique the concentration of live sperm/ml was relatively increased. Layering and swim up technique might avoid contamination of sperm in supernatant by pus cells & particulate matter. In selected cases this technique of sperm wash was used for IUI. In severe oligozoospermia IVF or for asthenozoospermia ICSI are the way outs. In our series pregnancy rate following IVF for male infertility was 25.58% and that following ICSI to be 22.6% which includes both ejaculated and aspirated sperm.¹⁴ (IRM data 2005 unpublished)

Azoospermia needs separate mention. All cases of azoospermia do not mean complete absence of sperm. Obstructive group may respond to reconstructive surgery with a limited success. Percutaneous epididymal sperm aspiration followed by ICSI (PESA-ICSI) may be helpful. Testicular atrophy demands artificial insemination with donor semen. In cases with primary testicular failure we directed the patients for donor insemination but for obstructive azoospermia epididymal sperm aspiration followed by ICSI was also rewarding. In selective cases of even testicular failure testicular sperm extraction (TESE) followed by ICSI may be helpful. When a man has azoospermia, it is the responsibility of the andrologist to determine whether testicular failure or obstruction is present. If the vas deferens is not palpable, unilaterally or bilaterally, then CF gene mutation testing is necessary. The most commonly encountered condition in this category is CFTR gene mutations, which typically manifests in azoospermic men with vasal or epididymal abnormalities. In RFC series the pregnancy rate in ICSI performed for severe
male infertility where only aspirated sperms (PESA, TESA, TESE) were used was 21.2% (clinical pregnancy) but the take home baby rate was 17.7% only. (RFC data 2002 to 2005 unpublished). \(^\text{15}\)

**OBSERVATIONS:**

The incidence of male infertility in our series was 30% amongst all infertile couples. The detectable factors, i.e. cases with known etiology were observed in 58 individuals (18%). Idiopathic group was the largest being 82% (Table I). The commonest type of defect found in our series was oligoasthenospermia. Other defects found in decreasing frequency were oligozoospermia, asthenozoospermia and others as given in Table II.

**TABLE II**

<table>
<thead>
<tr>
<th>DEFECTS</th>
<th>NUMBERS</th>
<th>PERCENTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>DETECTABLE FACTORS</td>
<td>116</td>
<td>18%</td>
</tr>
<tr>
<td>IDIOPATHIC</td>
<td>530</td>
<td>82%</td>
</tr>
<tr>
<td>OLIGOASTHENOSPERMIA</td>
<td>406</td>
<td>63%</td>
</tr>
<tr>
<td>OLIGOSPERMIA</td>
<td>138</td>
<td>21%</td>
</tr>
<tr>
<td>ASTHENOSPERMIA</td>
<td>64</td>
<td>10%</td>
</tr>
<tr>
<td>OTHERS</td>
<td>38</td>
<td>6%</td>
</tr>
</tbody>
</table>

**TABLE III**

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>NO OF CASES</th>
<th>IMPROVEMENT</th>
<th>PREGNANCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLOMIPHENE</td>
<td>116</td>
<td>52 (48%)</td>
<td>12 (10%)</td>
</tr>
<tr>
<td>GONADOTROPHIN</td>
<td>62</td>
<td>28 (46%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>ANDROGEN</td>
<td>156</td>
<td>54 (34%)</td>
<td>2</td>
</tr>
<tr>
<td>VITAMIN</td>
<td>418</td>
<td>220 (50%)</td>
<td>64 (15%)</td>
</tr>
</tbody>
</table>

Outcome of Clomiphene treatment is not encouraging (Table III)

Improvement in semen parameters after clomiphene treatment was in 48% cases but pregnancy could be achieved in only 10% of cases. This cannot be attributed only to clomiphene but in some cases female factors were also responsible. Gonadotrophin on
the other hand though showed improvement rate of 46% the pregnancy rate was not at all satisfactory. Androgens exhibited improvement in 34% cases with very poor pregnancy outcome. Vitamins i.e. Vit-E and B12 yielded better result where improvement was found in more than 50% cases and pregnancy was achieved in 15%. Above results indicate that vitamins are relatively more useful and less expensive.16

In severe seminopathy where medical treatment has no role assisted reproductive technologies which have been discussed previously were the method of choice. The outcomes are presented in table IV.

**TABLE IV (RFC data)**

<table>
<thead>
<tr>
<th>ART Procedures</th>
<th>No. of cases</th>
<th>No. of Cl. Preg</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI for severe seminopathy</td>
<td>210</td>
<td>16</td>
<td>7.5%</td>
</tr>
<tr>
<td>IUI for mild &amp; mod group</td>
<td>316</td>
<td>49</td>
<td>15.9%</td>
</tr>
<tr>
<td>IVF for mod to severe group</td>
<td>116</td>
<td>26</td>
<td>22.4%</td>
</tr>
<tr>
<td>ICSI for severe seminopathy</td>
<td>54</td>
<td>12</td>
<td>22.2%</td>
</tr>
</tbody>
</table>

Above results suggest that proper assisted reproductive techniques yield better pregnancy outcome.

**DISCUSSION**

The observations and results in our series are different from those reported in the literature. This is because oligoasthenozoospermia was the commonest aberration detected in our series. Isolated asthenozoospermia is a rare disorder. Drugs are ineffective for idiopathic oligozoospermia. Vitamins could improve oligoasthenozoospermia in about 50% cases but pregnancy rate remained low in our series. Vitamin has proved to be relatively more useful agent in our series. This is in contrary to the existing belief. What we have observed is vit E2 alone or in combination with vit B12 worked better in improvement of sperm motility. An excess of reactive oxygen species (ROS) and other oxidant radicals released by leucocytes particularly macrophages present in semen samples is associated with decrease in sperm motility. Antioxidants with the help of their oxyradical scavenging capacity can effect semen parameter improvement in selected cases. This is why asthenozoospermic samples did better with vitamins. On the other hand, vit B12 acts as coenzyme in many biochemical reactions in the production of
spermatozoa and also in its precursor and stem cells. This helps in improving sperm
motility and rarely in count too. In certain cases, which are not hormone dependent,
antiestrogens as stimulating agents may be successful. The main problem of clomiphene
is standardization of dose. It acts by stimulation of FSH secretion, which is not dose
dependent to clomiphene in the males. The antioestrogenic action of high dose
clomiphene may precipitate prostatic dysfunction as well as spermatid dysfunction in its
prolonged use. In the females the response to clomiphene treatment can be judged by
folliculometry and oestradiol estimation very shortly after starting the medicine, but in
the males monitoring of treatment takes prolonged period of 72-90 days when repeat
semen analysis determines the efficacy. In fact in many situations sperm count may
increase with clomiphene but not fertility. In few studies that did include control, the
investigators have concluded that clomiphene could be considered as an effective agent.
Use of gonadotrophin on regular basis is extremely costly. This may be physiological in
treatment of hypogonadotrophic hypogonadism. It is recognized now a days that 25%
cases of Idiopathic oligoasthenozoospermia is due to inadequate gonadotrophine activity
(IGA) when FSH and LH levels are normal in circulation. This is one of the main
indications of gonadotrophin use but the problem is the difficultly in confirmation of IGA
and it requires very high dose of gonadotrophin for treatment. The results of
gonadotrophin therapy are not also encouraging so far fertility of these men are
concerned.\textsuperscript{17}

With androgens particularly in low dose continuous treatment is helpful in some
occasions. High dose testosterone, which leads to complete suppression of
spermatogenesis followed by rebound stimulation of sperm production is also advocated
treatment with little improvement of fertility. Reproducibility of the rebound
phenomenon is also reported. The difficulties are the selection of treatment modality of
androgens for particular patients as there is no clear criterion for the same in the
literature. Therefore the results of androgen treatment are also poor\textsuperscript{21}.

Intra-Uterine Insemination (IUI), in many occasions of male factor infertility gives better
results than other modalities of medical management. In mild to moderate seminopathy
IUI gives better results so far pregnancy rate is concerned. The success rate of IUI varies
between 17\% to 20\% in unselected cases of mild to moderate seminopathy. When it is
done for severe seminopathy it is not more than 8\%. For such cases multiple frozen or
fresh pooled semen samples added together may lead to 10\% pregnancy rate. Though IUI
is widely practised in cases of male infertility meta analysis has clearly shown that IUI
has no benefit (The Capri ESHERE Workshop 1996). IUI has also been tried in cases of
obstructive azoospermia where in 25\% of such cases about 3 million motile sperms have
been retrieved through epididymal sperm aspiration (PESA) by the author and about 14\%
pregnancy rate could be achieved. In vitro fertilization needs about 100,000 motile sperm
to achieve a pregnancy. Now a days with the use of microdrop culture technique
insemination with 10,000 motile sperms nearly same rate of success can be obtained. This has helped many infertile males to father a child. The main drawback of the procedure is excessive cost involved and the time required for close monitoring. The psychological trauma of the couple is to be considered as well because the female partner has to bear all the burnt of treatment when the fault lies with male partner. The overall success rate of IVF is about 30% though in severe seminopathy the fertilization rate drops with less no of 2PN stage development.\textsuperscript{18,19}

The introduction of Intra Cytoplasmic Sperm Injection (ICSI) procedure that involves injection of a single spermatozoon into the cytoplasm of the oocyte has been the major breakthrough in management of male factor infertility. With the help of ICSI the male partner with severe seminopathy or even with azoospermia has about 33% hope of fathering a child. This highly specialized technique offers chance of parenthood to persons even with complete absence of spermatozoa through testicular retrieval of elongated or even round spermatids.\textsuperscript{20}

Oligozoospermia due to high seminal volume or even polyzoospermia often leads to infertility where medical management i.e., treating the person has no role to play. IUI that involves the minimum of manipulation at gamete level appears to be the only solution in these cases.

**CONCLUSION:**

Semen analysis still remains the primary investigation for the diagnostic and therapeutic approach of male infertility. The role of medical treatment in male infertility even though theoretically indicated is of minimum practical value. In moderate or mild seminopathies medical treatment is mostly done to buy some time and to give the couple to come to terms with the problems they are facing. Medical treatment may help in male sexual dysfunction. Sometimes corrective surgery for external genital organ defect may be of help. Gamete manipulation either for IUI or for IVF or for ICSI may yield acceptable pregnancy rate in couples with severe or untreated male infertility. Therefore the treatment of male infertility primarily involves his gamete and not the individual himself. It is now being increasingly recognized that genetic defect may be an important cause of many types of seminal defects. Hence while trying to achieve pregnancy through gamete manipulation the specific genetic defect affecting spermatozoa may be transmitted to a male offspring. Therefore proper counseling of the couple is mandatory while treating a male factor infertility through gamete manipulation. Lack of knowledge of aetiology mostly influences us towards use of medical treatment empirically which at the end of the day becomes ineffective and useless.
Acknowledgement

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REFERENCES:


