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ADVANCEMENTS IN MANAGEMENT OF INFERTILITY

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Abstract

Infertility can place a great pressure on relationship within a couple. Infertility problems have been a source of concern in India lately. The causes of infertility may be associated with male and female factors. Every effort must be made to offer infertile couples the best diagnostics paths. This article seeks to explain the treatment modalities specially the advancements in management of infertility. So that, most infertile couples will experience the joy of parenthood and help them ease the psychological and social implications related to infertility.

Keywords: Infertility, India, Management.

INTRODUCTION

Infertility is a source of social and psychological suffering for both men and women and can place great pressure on the relationship within the couple. Infertility affects approximately 13-14% of reproductive-aged couples. In 2010, almost 50 million couples worldwide were unable to have a child after five years of trying. Infertility rates have hardly changed over the past 20 years [1][1]. In U.S., one in six couples of childbearing age is affected by infertility. In 40% of cases, the problem is with the man; in 40% it's with the woman, and in 20%, something is amiss with both [2]. Infertility problems have been a source of concern in India lately. According to a 2013 World Bank estimate, the drop in fertility started about 10 years ago in India, with a steady 17 percent decline from the year 2000 [3]. Survey done by Indian Society for Assisted Reproduction revealed that out of 2562 participants 46% were infertile [4]. The WHO estimates the overall prevalence of primary infertility in India to be between 3.9 and 16.8 percent[5]. In this scenario, creating family by means of assisted reproductive technology, it has made a new dimension for distressed infertile couple.

Risk Factors for Infertility

The main risk factors for infertility are advancing age, late marriage, smoking, alcohol consumption, obesity, eating disorders, being vegan, over exercising and lack of exercise, sexually transmitted infections, exposure to some chemicals (some pesticides, metals) and mental stress [5].

Causes of Infertility

It may be due to male factors or female factors or may be due to both [6,7] (Figure 1& 2).

Diagnosis of Infertility

When evaluating an infertile couple, diagnostic studies should be selected as indicated.

Male factor testing

After a medical history and physical examination, semen analysis is the single best test for evaluating for male factor infertility. Chlamydia test and ultrasonography are also used for the diagnosis of male infertility. For optimum and consistent results, abstinence

is required 2-5 days prior to semen collection [8]. More recently, the Halosperm test and the Sperm Chromatin Structure Assay (SCSA) have been devised to evaluate the DNA fragmentation of sperm. Some studies suggest that a DNA fragmentation of greater than 30% is associated with a lower probability that the male partner will be able to initiate a pregnancy that carries to delivery [9].

Figure 1. Male causes

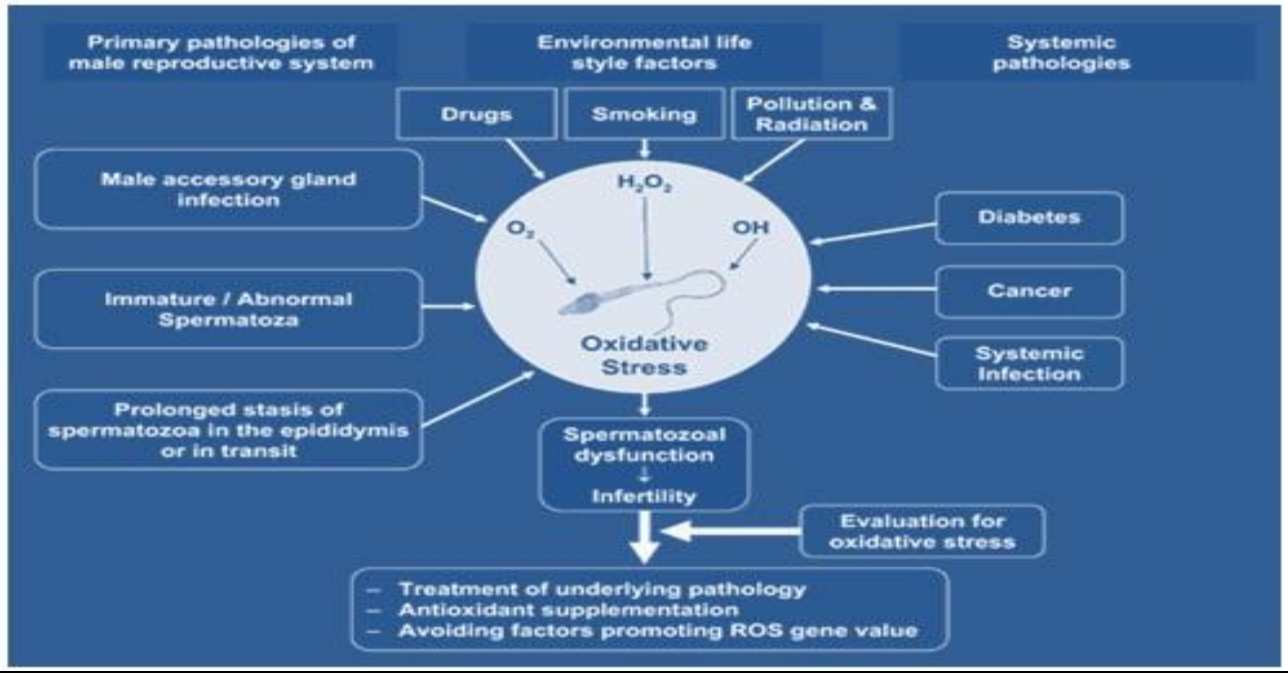
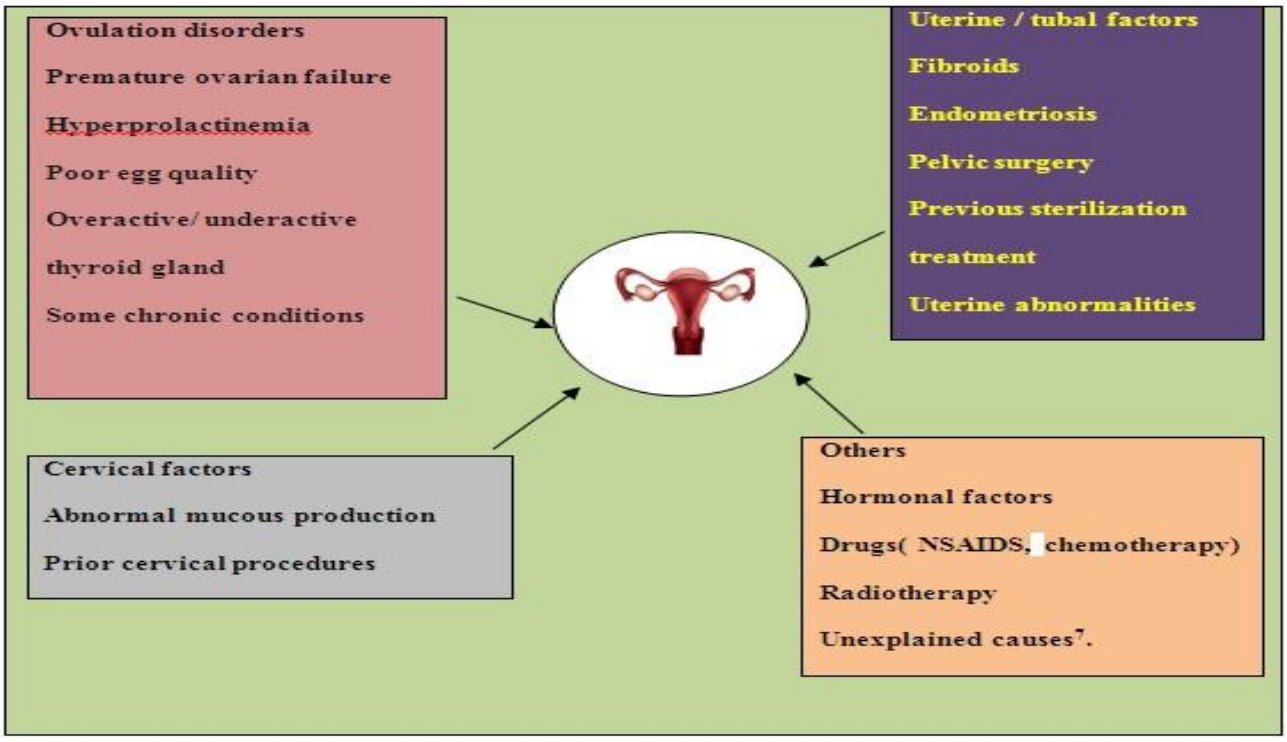


Figure 2. Female causes



Female factor testing

The diagnosis for female infertility includes general physical examination, estimation of hormonal levels, *Clomiphene Challenge Test, tissue samples, tests for autoimmune diseases, ultrasonography, hysterosalphingography, hysteroscopy and laparoscopy [7].*

Treatment

Treating the infertile client with competence and compassion is within the scope of practice for advanced practice clinicians. However, due to both a lack of emphasis on infertility treatment in many advanced practice education programs and confusion diagnosis and treatment by many practitioners, infertility is often undertreated by these providers [10].

FOR MEN

Limited numbers of medical treatments are aimed at improving chances of conception

Medical and hormonal remedies

A number of patients with hypogonadotropic hypogonadism respond to GnRH therapy or gonadotropin replacement. Patients with antisperm antibody levels greater than 1:32 may respond to immunosuppression using cyclic steroids for 3-6 months.

Electro ejaculation

Electro ejaculation is a procedure that is performed when a medical or psychological condition prevents a male from being able to ejaculate. Under general anesthesia, an unlubricated Foley's catheter is placed in the bladder and a buffer is instilled through the catheter. A rectal probe is inserted with its electrodes positioned against the posterior seminal vesicles. Electrical stimulation is begun at 3-5 volts and increased as necessary.

The Testicular Sperm Aspiration/Extraction (TESA/E); involves the direct removal of sperm from the testicles, which can then be used in conjunction with Intracytoplasmic sperm injection (ICSI).

Other

Repair of varicocele, vasectomy reversal, lifestyle modifications and dietary and vitamin supplements [11].

FOR FEMALE

Medical Management

Fertility drugs are often used alone as initial treatment to induce ovulation. If they fail as sole therapy, they may be used with assisted reproductive procedure

According to the American Society for Reproductive Medicine, fertility drugs can be divided into three main categories:

- *Medications for Ovarian Stimulation*. Clomiphene, letrozole, Follicle Stimulating Hormone (FSH), human Menopausal Gonadotrophin (hMG), Luteneizing Hormone (LH).
- *Medications for Oocyte Maturation*. human Chorionic Gonadotropin (hCG)
- *Medications to Prevent Premature Ovulation*. GnRh agonists, nafarelin (Synarel), and goserelin (Zoladex)]; Gn RH antagonists [ganirelix (Antagon), cetrorelix (Cetrotide)].

The commonly used drugs are; Clomiphene or Clomiphene Citrate

It causes the body to make more of the hormones that cause the eggs to mature in the ovaries. Clomiphene causes ovulation to occur in 80% of women treated. About half of those who ovulate are able to achieve a pregnancy or live birth. Use of clomiphene increases the risk of having a multiple pregnancy. There is a 10% chance of twins, but having triplets or more is rare—less than 1% of cases [12].

Gonadotropins and human Chorionic Gonadotropin (hCG)

Gonadotropins are hormones that are injected in a woman to directly stimulate eggs to grow in the ovaries, leading to ovulation. Health care providers normally prescribe gonadotropins when a woman does not respond to clomiphene or to stimulate follicle growth for ART. hCG is a hormone similar to leutenizing hormone that can be used to trigger release of the egg after the follicles have developed [12].

Bromocriptine or Cabergoline

Bromocriptine and cabergoline are pills taken orally to treat abnormally high levels of the hormone prolactin, which can stop ovulation. Certain medications, kidney disease, and thyroid disease can cause high levels of prolactin [12].

Surgical Treatment

If disease of the fallopian tubes is the cause of infertility, surgery can repair the tubes or remove blockages in the tubes. Success rates of these types of surgery, however, are low. Surgery to remove patches of endometriosis has been found to double the chances for pregnancy. Surgery can also remove uterine fibroids, polyps, or scarring, which can affect fertility [12].

Assisted Reproductive Techniques (ART)

One in six couples of any society remains infertile and 10% of them need help of Assisted

Reproductive Technology (ART). ART refers to all technology where gametes are manipulated outside the body. Bilateral tubal block, endometriosis, severe oligospermia, and azoospermia are the commonest indications for ART. Average pregnancy rate is 30%-34% worldwide [14]. The commonly used techniques are

Intra Uterine Insemination (IUI)

Intra Uterine Insemination (IUI) involves a laboratory procedure to separate fast moving sperm from more sluggish or non-moving sperm. The fast moving sperm are then placed into the woman's womb close to the time of ovulation when the egg is released from the ovary in the middle of the monthly cycle by a small catheter. The supplementation of luteal phase with vaginal progesterone significantly increases live birth among women undergoing IUI when receiving gonadotropins for ovulation induction [15].

***In Vitro* Fertilization (IVF)**

IVF is the most effective ART. It is often used when a woman's Fallopian tubes are blocked or when a man produces too few sperm. The basic steps in an IVF treatment cycle are ovarian stimulation, egg retrieval, fertilization, embryo culture, and embryo transfer.

Ovarian Stimulation

During ovarian stimulation, also known as ovulation induction, medications or "fertility drugs," are used to stimulate multiple eggs to grow in the ovaries rather than the single egg that normally develops each month. The common drugs used are, human Menopausal Gonadotropin (hMG), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), human Chorionic Gonadotropin (hCG) and clomiphene citrate.

Egg Retrieval

Egg retrieval is usually accomplished by transvaginal ultrasound aspiration, a minor surgical procedure that can be performed in the physician's office or an outpatient center.

Fertilization and Embryo Culture

After the eggs are retrieved, they are examined in the laboratory for maturity and quality. Mature eggs are placed in an IVF culture medium and transferred to an incubator to await fertilization by the sperm. Fertilization may be accomplished by insemination, where motile sperm are placed together with the oocytes and incubated overnight.

Assisted Hatching (AH) is a micromanipulation procedure in which a hole is made in the zona pellucida just prior to embryo transfer to facilitate hatching of the embryo. Pre implantation Genetic Diagnosis (PGD) is performed at some centers to screen for inherited diseases

Embryo Transfer

The next step in the IVF process is the embryo transfer. One or more embryos suspended in a drop of culture medium are drawn into a transfer catheter, a long, thin sterile tube with a syringe on one end. The maximum number of embryos transferred is based on the patient's age and other individual patient and embryo characteristics. Extra embryos remaining after the embryo transfer may be cryopreserved (frozen) for future transfer (cryopreservation) [17].

According to the most recent statistics from the U.S. Centers for Disease Control (CDC), about 31% of ART cycles (mostly IVF) with fresh embryos resulted in a live birth of one or more babies [3].

Intra Cytoplasmic Sperm Injection (ICSI)

Single sperm is injected into an egg to achieve fertilization during an IVF procedure. The likelihood of fertilization improves significantly for men with low sperm concentrations. ICSI may be used when a limited amount of sperm is available, such as in couples where the man has stored sperm prior to chemotherapy. ICSI is indicated in certain Pre implantation Genetic (PGD) Procedures—specifically those cases being evaluated for single-gene recessive disorders. This prevents the potential contamination of the specimen with sperm that may be attached to the egg[3].

Zygote Intra Fallopian Transfer (ZIFT)

During Zygote Intra Fallopian Transfer (ZIFT), oocytes are retrieved similar to IVF and GIFT and they are allowed to fertilize in vitro in the laboratory as in IVF. A day after fertilization (2 cell stage), 3-4 embryos are transferred via laparoscopy into one of the fallopian tubes [3].

Gamete Intra fallopian Transfer (GIFT)

GIFT is a technique devised to achieve pregnancies in most couples who have not been able to conceive using conventional treatments for infertility despite having good sperm and normal fallopian tubes. GIFT stands for "Gamete Intra-Fallopian Transfer". Gametes (i.e., the female's eggs and the male's sperm) are washed and placed via catheter directly into the women's fallopian tubes [14].

Blastocyst transfer

Blastocyst is an embryo that has developed for five to six days after fertilization. With blastocyst transfer, embryos are cultured in the laboratory incubator to the blastocyst stage before they are transferred to the womb [14].

Tubal Embryo Transfer (TET)

TET is a technique that combines IVF (In Vitro Fertilization) with a tubal transfer. TET stands for "Tubal Embryo Transfer". Embryos are placed via catheter directly into the women's fallopian tubes. This usually involves a minor surgical procedure that allows you to go home the same day with a minor degree of pain. TET allows embryos to make their way to the uterus for implantation according to a normal timetable. In contrast, IVF places embryos directly into the uterus. The success rate with TET is higher than standard IVF, but can only be performed if the woman has normal fallopian tubes. Its advantage over ZIFT is that it allows for the assessment of fertilization and embryo quality [14].

Elective Single Embryo Transfer (e SET)

Elective Single-Embryo Transfer (e SET) is a procedure in which one embryo, selected from a larger number of available embryos, is placed in the uterus or fallopian tube. The embryo selected for e SET might be from a previous IVF cycle (e.g., cryopreserved embryos (frozen)) or from the current fresh IVF cycle that yielded more than one embryo. The remaining embryos may be set aside for future use or cryopreservation [15].

Frozen Embryo Transfer (FET)

Embryo freezing, or cryopreservation, allows a couple to have additional attempts at assisted reproductive technology without the expense of ovulation induction and having to undergo an additional egg retrieval procedure. A frozen embryo transfer allows for a second, third or more chances at conceiving from the original cycle [14].

Donor sperm, eggs, and embryos

IVF may be performed with a couple's own eggs and sperm or with donor eggs, sperm, or both. A couple may choose to use a donor if there is a problem with their own sperm or eggs, or if they have a genetic disease that could be passed on to a child. Donors may be known or anonymous.

Surrogacy/gestational carrier

A pregnancy may be carried by the egg donor (traditional surrogate) or by another woman who has no genetic relationship to the baby (gestational carrier). If the embryo is to be carried by a surrogate, pregnancy may be achieved through insemination alone or through ART [3].

Most unsuccessful in vitro fertilization cycles fail after embryo transfer, so research has focused on trying to identify the best embryos to transfer. Non-invasive ways to assess the embryo's health have looked at the embryo's metabolism—in particular the amino acid profile. Metabolically quiet embryos are more likely to develop than those with a high amino acid turnover [13].

Psychological and ethical implications related to infertility

Every medical, social, and political effort must be made to prevent infertility but also to offer infertile couples the best diagnostic and therapeutic paths. Understanding the suffering of the couple and their families prevents and helps ease the possible psychological and social complications of infertility. Therefore, infertility concerns not only biomedical sciences but also psychological and social ones—ethics and law—in their combined efforts to identify areas of understanding and of research for solutions while respecting the dignity of the couple and unborn child [17].

CONCLUSION

The decision to seek treatment for infertility is a viable one due to the assisted reproductive technologies available today. With patience, a positive attitude, and the appropriate treatment, most infertile couples will eventually experience the joys of parenthood.

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