Female Sexual Dysfunction and Infertility

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Infertility is defined as the failure to achieve pregnancy after 12 months or more of appropriate, timed unprotected intercourse or donor insemination [1]. Women who are over age 35 are encouraged to initiate an evaluation after only 6 months of trying to become pregnant due to the lower probability of achieving pregnancy each month compared to younger women. This recommendation stems from the shorter window of remaining reproductive potential when compared with younger women. In couples in whom known or suspected infertility risk factors may be present, i.e., history of irregular periods, severe endometriosis, factors that predispose to tubal occlusion such as pelvic inflammatory disease, or a known or suspected male factor like undescended testicles or prior chemotherapy, an evaluation may be initiated after only 3 months of trying.

While initial attempts to conceive often start as "let's just see what happens when we stop using contraception" and possibly an increased frequency of sex, the frustration and anxiety of failed conceptions quickly escalate after each menstrual period, resulting to a methodical and planned scheduling of one's sex life around anticipation of ovulation and the "fertile window." The myth that a couple will have sex once and get pregnant or that pregnancy should happen the first month you try despite advancing age of the female partner is unfortunately a widely held belief. The most important factor in determining a woman's eventual chances for conception is her age. A German study evaluating time to pregnancy in couples stopping natural family planning methods documented a cumulative probability of pregnancy of 38 %, 68 %, 81 %, and 92 % at one, three, six, and 12 cycles, respectively, [2]. Most couples conceived within 6 months of trying. In women undergoing donor insemination due to a severe male factor such as azoospermia, pregnancy rates after up to 12 cycles of insemination with donor sperm were 74 % in women <31 years of age. The negative impact of age on fertility was clearly evident as women >35 years of age had a pregnancy rate of only 54 % after 12 months of appropriately timed donor insemination.

29.1 Evaluation

In couples who fail to conceive, a thorough evaluation of identifiable and potentially correctable causes of infertility should be initiated. This starts with a history and physical examination. Most couples are referred to an OB/GYN or reproductive endocrinologist, a physician trained to focus

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on abnormalities of the female reproductive tract, and the conversation usually starts with a complete menstrual and gynecologic history of the female partner. Questions regarding the woman's menstrual cycles and symptoms may provide information about ovulation, while questions pertaining to prior gynecologic problems including abnormal PAP smears, sexually transmitted infections, surgeries, and even prior pregnancies with other partners may reveal anatomic conditions reducing chances of pregnancy. Questions to both partners then focus on other risk factors including medications, exposures to reproductive toxicants like smoking or chemotherapy, as well as family history. Men are asked to provide a semen sample for analysis. If normal, other than the initial semen analysis and providing sperm when needed (which can even be cryopreserved for future use), the remainder of the evaluation and treatments falls on the female partners' shoulders to endure.

The examination of the woman includes, but is not limited, to an examination of her thyroid gland and breasts for secretions or masses, pelvic examination, cervical cultures, and transvaginal sonogram to assess ovarian "reserve," a measure of the relative quality and quantity of follicles remaining (albeit not a very accurate marker). If an identifiable etiology of infertility can be determined, directed measures to correct the abnormality may be undertaken depending on the chances of success. For example, if tubal pathology is identified in a 38-year-old nulligravid woman and surgical correction yields a 20 % probability of conception after 12 months with 25 % of all conceptions being tubal ectopic pregnancies, the decision to forgo surgery and proceed to IVF or remove the fallopian tubes to improve the odds of IVF being successful would be reasonable.

Testing for identifiable and correctable causes of female factor infertility is relatively straightforward and should not take more than a single cycle to complete. The testing falls into three main buckets: hormonal (ovulation and luteal function post-ovulation), anatomic factors (cervical abnormalities, endometrial defects, and tubal/peritoneal factors), and egg factors (advanced age with diminished egg quantity and anticipated high rate of oocyte aneuploidy). Testing for these factors includes documentation of ovulatory cycles, which can be obtained from the history and is supported by the patient having regular menstrual cycles with molimina. Infertility in up to 15 % of all infertile couples and up to 40 % of infertile women is due to ovulatory disturbances [3]. In the presence of regular cycles, a serum progesterone level, basal body temperatures, urine LH testing, and especially endometrial biopsy are unnecessary.

Anatomic abnormalities are detected with a hysterosalpingogram (HSG), during which radiopaque contrast is injected into the uterine cavity and fluoroscopy confirms the shape of the uterine cavity and identifies any anatomic defects as well as spillage of dye from the fallopian tubes into the peritoneal cavity, consistent with tubal patency. If performed properly, rarely will there be false-positive or false-negative interpretations which would require surgery to confirm. In the presence of a normal HSG, laparoscopy is not indicated. Cervical factors, including abnormalities of cervical mucus, have traditionally been evaluated with a "post-coital" test where a sample of the peri-ovulatory cervical mucus is looked at under a microscope within 12 h post-coitum. The presence of motile sperm in the setting of thin, watery "egg white"-like mucus is considered a normal result. However because the findings correlate poorly to the ability to conceive a pregnancy, this test is no longer recommended [4].

Ovarian "reserve," a measure of the quantity and quality of remaining eggs, is also difficult to determine. The most predictive variable in a couple's ability to achieve pregnancy is chronologic age of the female partner. Advanced age of the female partner, independent of oocyte quantity, is the best predictor of artificial reproductive technology (ART) outcome. Surrogate markers for ovarian function include cycle day 3 follicle-stimulating hormone (FSH) and estradiol levels as well as anti-Müllerian hormone (AMH) levels. High-frequency ultrasound can also provide an objective measure of quantity of antral follicles in the ovary and a close correlation with total number of retrievable oocytes. High levels of AMH indicate a larger number of potentially

recruitable eggs similar to a higher antral follicle count (AFC). High levels of FSH, on the other hand, indicate diminished ovarian reserve and fewer potential oocytes. However, the threshold for FSH as a marker of ovarian reserve has not been determined, and there is high intra-cycle variability in FSH levels, limiting its utility in fertility evaluation in women. At this time, none of the ovarian reserve markers, unless a very high threshold is used, have a strong correlation with pregnancy outcome.

29.2 Treatment

When a specific abnormality can be identified, treatment can be directed at correcting the abnormality, i.e., tubal pathology can be surgically corrected or bypassed with in vitro fertilization. Having a diagnosis, however, even if not correctable, makes treatment easier to undergo. An etiology of infertility is not identified in up to 30 % of couples and even more if considering those couples in whom a diagnosis is made, but treatment remains ineffective [5]. In some, the diagnosis is merely reduced cycle fecundity due to advanced age of the female partner and pregnancy rates are expected to be low. A common but ineffective treatment for infertility is intrauterine insemination, where washed and concentrated sperm are placed high into the uterus, bypassing the need for the sperm to travel through the vagina and cervix. Pregnancy rates using IUI and those from timed intercourse are low: 4.8 % with IUI and 2.1 % with timed intercourse or intracervical insemination [6].

Because the chances for pregnancy with a single egg developing each month are low, most infertility treatments are aimed at stimulating multiple follicles to develop and mature in the hopes of increasing the chances that at least one will fertilize and implant; this process is termed ovulation induction. First-line therapy is often in the form of oral medications that antagonize the production of, or response to, estrogen. Clomiphene citrate (CC), a weak estrogen, stimulates FSH secretion and follicle development by blocking the estrogen receptor, while letrozole, an aromatase inhibitor, blocks the production of estrogen. Neither agent has proven superior over the other, but pregnancy rates remain quite low per cycle for both drugs. With CC alone, cycle fecundity rates were 5.6 %, and the combination of CC/IUI increased cycle fecundity rates slightly to 8.3 % [6]. Cycle fecundity rates with daily injections of FSH (gonadotropin) for 2 weeks to facilitate egg maturation were 8 % per cycle and 18 % per cycle when IUI was performed in addition to the use of ovulation-inducing medications [7]. It should be considered that the anticipated success of each subsequent treatment declines with each failed cycle, so the above success rates per cycle do not continue indefinitely.

While ovulation induction seems to be a reasonable approach to enhancing fertility, there are risks associated with this process, with the greatest risk involving the possibility of multiple gestations. In fact, this approach is responsible for many more twins and triplets than IVF [8]. Clomiphene citrate treatment results in a twin pregnancy rate of ~8 to 10 % and gonadotropin treatment increases this to ~33 % [7, 9]. IVF is an effective treatment for infertility due to all causes of infertility except for uncorrectable uterine factors and advanced female age. Success rates per cycle are 40.1 % at <35 years of age and decrease to 21.2 % between 38 and 40 years of age and 4.5 % in women over 42 years old [10]. Given unlimited resources and time, cumulative success rates would be rather good with the majority of younger couples achieving their goal of having one or more children. Unfortunately this is often not the reality. Each cycle of ovulation induction involves multiple, almost daily blood tests, transvaginal ultrasound examinations, and hormone injections. If that does not reduce the desire for intimacy with your partner, knowing that until the developing eggs are ready there is no reproductive purpose to having sex usually significantly decreases sexual desire. For this reason, FSD is common in women experiencing infertility.

Studies have linked the physical, psychological, and financial challenges of assisted reproduction to increased marital conflict, decreased sexual self-esteem, feelings of inadequacy, and decreased

frequency of sexual intercourse [11, 12]. Women struggling with infertility experience greater levels of psychosocial distress than men with respect to grief, guilt, denial, anxiety, cognitive disturbance, depression, and hostility [13]. More often women initiate medical treatment for infertility and are more invested in having a child. Typically, women are more aware of the limits of their reproductive potential and are more willing to consider extreme or alternative measures to achieve parenthood than their partners. For women, reproduction and sexuality may be more intrinsically intertwined than they are for men, so that disturbances in one area reverberate in other areas [14].

Sexual dysfunction is high in all infertile women, and women with secondary infertility suffer more from impaired sexual function than those with primary infertility [15]. Various studies have detected increased sexual dysfunction in 40–62 % of infertile women and reported loss of desire and arousal as the leading cause of dysfunction [14, 16–19]. Overall, infertility is associated with decreased sexual activity and appears to become worse as the number of childless years increases [20].

It has been speculated that three factors operate together in driving women's distress level higher than their spouses' [21]. First, the social responsibility of conceiving and pregnancy is still attributed mainly to the female partner [22]. Women often feel failure with regard to sexual and reproductive functions (further reinforced by medical terminology such as premature ovarian "failure" or "incompetent" cervix). Women view the role of mother as an integral part of their femininity, gender identity, and sexuality. Consequently, anything that threatens this role has the potential for negative social pressure and internal conflict.

Second, fertility treatment is more intrusive, time consuming, and often painful for women than it is for men [21, 22]. Infertility-related stress for women can be associated with not only the diagnosis but also treatment procedures, many of which are physically, psychologically, or pharmacologically invasive. Sexual intercourse can lose its spontaneity and erotic value as the goal becomes pregnancy, and sex becomes restricted to fertile times of the month [23]. This distortion of a sexual relationship can be long lasting and even cause disruptions to a couple's sexual life long after treatment [24].

Finally, coping strategies differ between men and women: men tend to deny and remain active, while women cannot imagine life without children and develop depressive reactions [21, 22]. Researchers found that positive reinterpretation and active coping strategies had a positive impact on sexual functioning, while planning and self-restraint coping had an adverse effect on sexual functioning [25].

The link between infertility and sexuality is complex. Sexual dysfunction may have an etiological role in infertility, or it may be a consequence of the disorder secondary to psychological stress in either or both partners. Regardless of the cause of infertility, research has consistently shown that in response to infertility and its treatment, women experience greater emotional distress than men and often assume more personal responsibility while enduring a disproportionate share of medical treatment [14]. In short, infertility clearly impacts the sexual functioning and sexual health of women in numerous ways.

29.3 Infertility Leading to Sexual Dysfunction

Women undergoing fertility treatment characterize infertility as the most stressful experience of their lives [26–28] likely contributing to higher reported rates of depression and sexual dysfunction [29, 30]. Sexual impairment in infertile couples is often due to the performance pressure experienced in response to planned sex, pressure to perform on demand, extensive and painful tests, intense feelings of anxiety, and the highly personal matter of sexuality being turned over to the external control of a physician and the psychological feeling of the medical team in the bedroom [31, 32]. As infertility drags on, feelings of sexual inadequacy and depression can occur due to the close association between sexuality and fertility [33].

Couples in infertility treatment report avoiding sexual intimacy during non-fertile times. Men and women lose pleasure from non-procreative sexual activity and develop an apathetic attitude about sex [34]. Similarly, women with tendencies to hypoactive sexual desire may find themselves avoiding sex except when they are ovulating or avoiding foreplay in order to facilitate a more rapid ejaculation from their partner. Regrettably and all too frequently, relationship building and recreational aspects of sexual activity are abandoned especially when large sums of money and sometimes invasive procedures are employed to induce ovulation. Sex on demand and providing an erection and ejaculation that is timely and efficient become the goals of sex [14, 35]. These tensions frequently lead to a reduction in nonsexual affection, resulting in feelings of disconnection and exacerbating relationship tension [36].

29.4 The Evaluation and Treatment of FSD and Infertility

It is clear that the stress, psychological demands, and physically intrusive procedures associated with infertility treatment can affect sexual self-image, desire, and performance. Whether sexual dysfunction is a preexisting condition or an unwelcome side effect of infertility treatment, it can be a devastating and discouraging blow, compounding the disappointment of childlessness and the distress of medical treatment.

Most infertile couples are reluctant to discuss the private sexual aspects of their relationship, but even more so when they fear it will interrupt medical treatment [37]. Consequently, the sexual problems of infertile couples are ignored or minimized in a belief that they will dissipate on their own or will have few long-term consequences. Unfortunately, although some sexual problems may disappear when the pressures of infertility treatment end, sexual difficulties may linger or become more problematic after treatment ends or parenthood is achieved [21, 22].

Even couples who never encounter major or disrupting sexual problems often experience episodic or situational diminished sexual desire and satisfaction in response to the emotional distress or physical strains of infertility or a specific treatment. Episodic loss of desire in one or both partners can usually be addressed with minimal education and reassurance. However, consistent and extensive diminished sexual desire in infertile men and women is more problematic and usually multifactorial.

Numerous partner-related psychosexual issues may adversely affect outcome. Contextual factors, including difficulties with the current interpersonal relationship, should be clarified, and previous sexual scripts should be assessed [14]. Preexisting psychiatric conditions as well as psychological issues that develop as a result of an infertility diagnosis and/or treatment should also be evaluated and addressed.

Ideally, if the sexual problems reflect more fundamental relationship problems, it may be more important that those issues take precedence over further infertility treatment. However, questions about whether treatment should be denied or postponed often pose very real dilemmas for medical caregivers and for infertile couples, especially if couple's fixation on parenthood clouds their judgment about the health and well-being of their marriage, family, their potential children, and themselves [14].

Sex therapists can assist fertility specialists and can intervene on several different therapeutic levels by providing patient education and helping patients with treatment decisions. Although some patients may proceed with infertility treatment in the presence of some sexual dysfunctions, medical treatment should be in conjunction with psychotherapy and/or sex therapy, emphasizing the importance of sexual health and well-being in infertile couples.

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