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The association of sexual dysfunction and male infertility: a literature review

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Abstract

Introduction: Sexual dysfunction and male infertility are important issues concerning men's health and reproductive potential. The relationship between these two conditions is complex and needs careful consideration. In this paper, we will look at how sexual dysfunction affects male fertility, looking at risk factors, why it happens, and ways to deal with it. This topic is important, as understanding it, can help improve men's health and increase the chances of successful reproduction.

Purpose: The purpose of this paper is to examine the relationship between sexual dysfunction and male infertility. An effort is made to understand how sexual dysfunction affects men's ability to reproduce, while examining risk factors, causes, and available treatment approaches.

Methodology: The methodology includes the analysis of the available literature, the collection and analysis of data from scientific studies, as well as the examination of the various methods of diagnosis and treatment of sexual dysfunction and male infertility.

Results: Analysis of the literature reveals significant associations between sexual dysfunction and male infertility. Scientific studies provide evidence of the causes and treatment options available.

Conclusions: Research papers on sexual dysfunction and male infertility reveal the importance of diagnosing and treating these problems for male health and reproductive capacity.

Keywords: Sexual dysfunction, male infertility, sexual health, infertility, male reproductive system

Introduction

Sexual dysfunction and male infertility are two major and complex issues that affect men's sexual health and reproductive capacity. On the one hand, sexual dysfunction refers to problems that a man may experience during the different stages of the sexual act, most notably premature ejaculation, erectile dysfunction and hypoactive sexual desire disorder. It affects more than 50 percent of males above the age of 40 (Anderson,2022). The causes may be both organic and/or psychological. Comorbidities, namely arterial hypertension, diabetes mellitus, as well as hormonal disturbances, are included in the most common risk factors for developing sexual dysfunction. Furthermore, lifestyle parameters such as exposure to toxins, excessive smoking and alcohol consumption may be associated with impaired sexual function. Anxiety and depression may also contribute alone or in combination with the aforementioned risk factors.

On the other hand, male infertility is related to a man's inability to produce healthy spermatozoa and participate in the process of reproduction. Up to 2019 it was estimated that more than 56 million men are affected (Huang, 2024). Problems in spermatogenesis, anatomical disorders of the male reproductive tract, chromosomal abnormalities, genetic mutations, and hormonal disturbances are some of the causes leading to infertility in men. Also, infections from specific pathogens, exposure to pollutants, as well as legal and/or recreational drug use are factors that should be taken into notice.

Early diagnosis and management of both sexual dysfunction and male infertility is of outmost importance. Fortunately, nowadays there are plenty of laboratory tests and imaging methods by which these issues can come to light. The therapeutic options are also various and can be either non invasive in the form of medications and counseling or invasive in the

form of surgery depending on the cause. In this review we will try to address all the above mentioned parameters in further detail.

Male Infertility

The male reproductive system comprises of both internal and external organs. The external organs consist of the scrotum and the penis, and the internal organs include the testes where the sperm is produced, the epididymis, the vas deferens ,the seminal vesicles, the bulbourethral glands and the prostate. Testosterone, which is the major male androgen, is produced in the testes by the Leydig cells and is involved in the development of primary and secondary sexual characteristics. Therefore, it is responsible for the growth of the penis and the descend of the testes in the gestational period, as well as of the deepening of the voice during puberty, the increased hair growth, and the increase in the muscle mass among others, in the male population. (Nassar & Leslie, 2023) (Griffin & Wilson, 2001). Testosterone, being one of the hormones of the hypothalamic-pituitary-gonadal axis along-side FSH and LH, is also responsible for the spermatogenesis and is highly involved in male fertility. There many studies in the last 40 years involving the different signaling pathways taking place in the Sertoli cells of the testes that mediate the spermatogenesis, including the AR(androgen receptor), cAMP/PKA and PI3k/Akt pathways (Ni, 2020). Testosterone levels decline gradually over time with aging (Harman et al., 2001) affecting the male's fertility potential.

Infertility in men refers to the inability of the male organism to cause pregnancy to a woman, despite frequent and unimpeded sexual intercourse within one year (Gurunath et al., 2011). There are many factors that can lead to male infertility.

Firstly, problems in spermatogenesis, such as no sperm production (azoospermia), insufficient sperm

production leading to low sperm counts (oligospermia), reduced motility (asthenozoospermia), or problems with the morphology of the sperm (teratozoospermia), can affect the reproductive capacity. There can be also a combination of those, known as OAT syndrome, that can lead to reduced fertility (Tüttelmann, 2018).

Chromosomal abnormalities also affect spermatogenesis, with typical examples being Klinefelter syndrome (47,XXY), and Jacobs syndrome (47,XYY). (Tüttelmann, 2018). The extra X- chromosome in Klinefelter syndrome has been associated with hyalinization and fibrosis of the testes, that result in hypogonadism (Los, 2013). On the other hand, the extra Y-chromosome in Jacobs syndrome is linked to congenital anomalies of the male reproductive system such as cryptorchidism, hypospadias, and hypoplastic scrotum and microphallus. All these may lead to oligospermia (Sood, 2022).

Furthermore, genetic mutations involving the TEX11, DMRT1, and NR5A1 genes, also referred as the “male infertility genes”, in recent studies have been associated with azoospermia (Tüttelmann, 2018).

Anatomical disorders of the male reproductive tract are also an important cause of male infertility. Mainly they involve ejaculatory tract obstruction problems or blood supply disturbances in the testes. As far as ejaculatory duct obstruction is concerned, it can be caused by either congenital abnormalities, such as agenesis and atresia of the ejaculatory duct, or acquired in cases of trauma, infections and surgical procedures in the pelvic region (Achermann, 2021). Dilation of the veins of the pampiniform plexus in the testes, also known as varicocele, can impact spermatogenesis via many mechanisms including oxidative stress, heat stress, hormonal imbalances, testicular blood stasis and hypoperfusion (Clavijo, 2017). All these types of anatomical disorders can limit the production, transport or release of spermatozoa.

On hormonal level, endocrine disorders can also

impact male fertility. Specifically, disorders affecting on different levels the hypothalamic-pituitary-gonadal axis, either by excess or lack of hormones, can lead to subfertility or infertility. Typical examples are hypogonadotropic hypogonadism, hypergonadotropic hypogonadism, hypothyroidism, hyperthyroidism, hyperprolactinemia, diabetes mellitus, high levels of androgens, testosterone deficiency, and excessive estrogen levels. (Sengupta,2021).

Another factor that affects male fertility are bacterial and viral infections. Pathogens that impact on sperm motility and quality, as well as spermatogenesis, causing tissue inflammation, are *Cl.trachomatis*, *N.gonorrhoeae*, *U.urealyticum*, *E.coli*, *S.aureus*, *Ps.aeruginosa* and *Brucella* (Wang, 2021). Viruses that have been associated with male infertility include Influenza virus, Mumps virus, HIV, HSV, viral hepatitis and HPV (Akhigbe, 2022). Oxidative stress and autophagy are the main mechanisms by which these bacteria and viruses function.

Recent studies have shown that tobacco use, alcohol consumption and recreational drug use can impair spermatogenesis, sperm count, quality, morphology and motility. They also act on a hormonal level, affecting the hormones of the hypothalamic-pituitary-gonadal axis. (Sansone, 2018). Drugs used for chronic diseases, mainly neoplasms, cardiovascular diseases, Parkinson, depression and epilepsy, and also specific anti-inflammatory drugs and antibiotics act by the same foretold mechanisms, also causing fertility problems. (Ding, 2017)

Lastly, exposure to environmental pollutants and occupational hazards may lead to male infertility. Ionizing radiation, chemicals, air pollution and heavy metals are responsible for sperm quality and quantity disorders (Abdoli, 2022)

Male Sexual Dysfunction

Sexual dysfunction in males involves a series of

problems related mainly to ejaculation and/or erection during the sexual act, or it can be acquired. (Anderson, 2022). Although in order for erection and ejaculation to take place, sexual arousal must precede. According to Master & Johnson there are four stages of the sexual response cycle. On the first level is excitement, also known as arousal, in which a variety of stimuli activate the parasympathetic nervous system leading to vasodilation of the arteries supplying the penis and increase in its muscle tone, resulting in an erection. On the second stage is the plateau, where the erection is further intensified. On the third stage, orgasm takes place. Orgasm refers to the feeling of intense pleasure during the sexual act. In most cases, during this stage ejaculation occurs. The ejaculation itself has two phases: the emission and the expulsion phase. Lastly, on the fourth stage, also known as the resolution period, the body returns to the state before the arousal took place. (Arwaal, 2015) (Master & Johnson, 1966) (Hirsh, 2022).

The most common conditions associated with male sexual dysfunction are erectile dysfunction, premature ejaculation and hypoactive sexual desire. Erectile dysfunction is an important and frequent problem among the male population. It is the inability of a man to achieve or maintain an erection sufficient to perform the sexual act with satisfaction. (Feldman, 1994). There are many factors that can lead to erectile dysfunction. They can be organic and/or psychological.

Organic factors include chronic systemic conditions such as arterial hypertension, diabetes mellitus, and cardiovascular diseases, which affect the function of the endothelial cells of the vessels. (Leslie, 2024). Lifestyle parameters, including excessive alcohol consumption and smoking, have an additive effect to the aforementioned comorbidities, by furthering the endothelial damage and decreasing the levels of nitric oxide which causes vasodilation to the penile arteries. (Kovac, 2015) (Li, 2021).

Psychological factors, on the other hand, such as stress, depression, emotional disorders, and problems within the relationship can cause erectile dysfunction. Age is also a frequent factor, as erectile dysfunction increases with advancing age (Shamloul, & Ghanem, 2013).

Premature Ejaculation

Premature ejaculation is a common sexual dysfunction that affects many men at different stages of their lives. It is the inability of the man to control the time of ejaculation during the sexual act. Men with this type of disorder either ejaculate almost always too quickly, which is less or about 60 seconds after first vaginal penetration (lifelong premature ejaculation), or have short intravaginal ejaculatory latency time of about 3 minutes or less in duration at any sexual encounter (acquired PE). (Althof, 2014) (Waldinger, 2008).

Premature ejaculation is usually caused by a combination of factors, including physical and psychological factors. The neurotransmitter serotonin normally delays ejaculation. Low levels have been associated with premature ejaculation (Waldinger, 1998). Another organic cause involves the thyroid function. Hyperthyroidism has been linked to premature ejaculation by inducing low libido or anxiety (Carani, 2005). Furthermore, bacterial infections and chronic inflammation of the prostate gland can also lead to ejaculation problems (Shamloul, 2006). Alcohol dependence and frequent use of recreation drugs and opioids are also a risk factor associated with premature ejaculation as they affect the levels of androgen production and the levels of FSH and LH, which belong to the hypothalamus-pituitary-gonadal axis (Acharya, 2022) (Grover, 2014).

On the other hand, psychological factors, such as depression and emotional stress can worsen premature ejaculation (Althof, 2014). This can lead to increased stress, isolation from the perspective

romantic partner and problems with self-image (Mourikis, 2015).

Hypoactive Sexual Desire Disorder

Hypoactive sexual desire disorder is a sexual disorder that affects a person's ability to show adequate sexual desire and interest in sexual activities (American Psychiatric Association, 2013). The causes of low libido are complex and varied. Usually, they combine physical and psychological factors.

Physical factors may include hormone levels, such as low testosterone, high prolactin or thyroid hormone disorders (Atis et al, 2011), which affect sexual desire. Both hypothyroidism and hyperthyroidism have been linked to impaired libido. (Gabrielson, 2019). As far as prolactin is concerned, high levels of this hormone inhibit the secretion of gonadotropin-releasing hormone in the hypothalamus, therefore decreasing the testosterone levels in the organism, leading to not only erectile dysfunction but to also low sexual desire (Zeitlin, 2000) (Corona, 2004).

Psychological factors, such as depression, anxiety, problems within the relationship and body image, are also often associated with low libido (Corona, 2005). Furthermore, childhood trauma can have serious effects on an individuals' sexual functioning. People who have experienced sexual abuse in childhood are more prone to experience sexual dysfunctions such as erectile dysfunction and hypotonic sexual desire (Noll, Trickett, & Putnam, 2003).

Diagnosis

The evaluation of male infertility and sexual dysfunction includes a series of medical examinations and laboratory tests aimed at assessing male reproductive capacity. The first diagnostic examination usually involves gathering information about the patient's history, including past illnesses, medication use, alcohol or drug use, and other conditions that

could be associated with sexual dysfunction (Montague et al., 2005). Questionnaires that assess symptoms, such as the IIEF-5 (International Index of Erectile Function) are also widely used (Forbes, 2017). Psychological evaluation also may be necessary. Psychologists and psychiatrists assess the individual's psychological state, as well as anxiety or depression (Althof et al., 2014).

From the laboratory point of view, semen analysis assesses sperm concentration, motility and shape, as well as sperm volume (Carlsen et al., 1992). Specifically, the quantitative evaluation is done through a spermogram and includes the calculation of the total number of sperm per volume unit (ml). Regarding the semen quality, morphological assessment focuses on evaluation of the regularity of the shape of the spermatozoa, while motility assessment analyzes their ability to move propulsively (Mortimer, 2017). Other laboratory tests used for the evaluation of male fertility include hormonal measurements. Measurements of the levels of testosterone, follicle stimulating hormone and luteinizing hormone in blood can help identify potential endocrine disorders that may be affecting fertility. (Sikka,2016). In cases of chromosomal disorders, karyotyping for the detection of deletions, translocations and duplications, is essential (Stormont, 2021). Gene sequencing may also aid in diagnosing specific abnormalities. (Tüttelmann, 2018)

As far as imaging methods are concerned, scrotal, penil and transrectal ultrasounds can highlight both anatomical and acquired disorders affecting male infertility, by assessment of the testicles, the penis, the epididymis, the vas deferens, and prostate gland. Testicular venography is also used in cases of varicocele, but is an invasive method (Ammar, 2012). Another invasive method used for further assessment of male fertility, especially in cases of unexplained infertility because of malignancies of the genitourinary tract, is tissue biopsy (Dohle,2012).

Treatment

Treatment of sexual dysfunction

There are several therapeutic options as far as sexual dysfunction is concerned both in the form of medications and surgery, as well as and in the form of psychotherapy.

Firstly, 5-Phosphodiesterase Inhibitors are the most common and popular choice for the treatment of erectile dysfunction. The most common drugs of this category are Viagra (sildenafil), Cialis (tadalafil), and Levitra (vardenafil) (Goldstein et al., 1998). Another form of treatment involves the injection of a mixture of papaverine-phentolamine and prostaglandin E1 before sexual activity. Both these types of medication work by increasing the blood flow to the penis and can help achieve and maintain an erection. (Fallon, 1995). Infusion of autologous activated platelets (PRP), as well as stem cell infusion (SCT) via injection to the penis have also been used to treat erectile dysfunction, as they aid cellular and vascular growth (Israeli et al., 2022). Furthermore, studies have shown that selective serotonin reuptake inhibitors, such as Dapoxetine, Paroxetine, Fluoxetine, and Sertraline, have shown effectiveness in cases of premature ejaculation with little side effects and good general tolerance. (Siroosbakht, 2019) (McMahon, 2011)

In cases where sexual dysfunction is related to low testosterone levels, testosterone replacement therapy can help improve erectile function. (Nieschlag & Behre, 2012). There are several routes via which testosterone can be administered. It can be taken per os, via injection intramuscularly, transdermally, intranasally, and subcutaneously. Except testosterone, derivatives of it are also used, such as testosterone undecanoate, which in several studies has shown better long term effects (Campbell, 2023). It is worth mentioning though, despite the benefits in erectile function, libido and quality of life, there are several

side effects linked to testosterone replacement therapy, such as liver toxicity, erythrocytosis, arterial hypertension, increased risk of prostate and breast cancer in males, and even infertility. Due to the aforementioned risk factors, close and regular follow-up of these patients is recommended. (Osterberg, 2014).

On a surgical basis, treatment of sexual dysfunction may involve Penile Prosthesis. During this procedure, penile implants are inserted, which can induce an erection at the patient's will (Mulcahy, et al., 2004), (Gross et al., 2016). Currently, two types of prostheses are used: the semirigid endoscopic prosthesis (malleable) and the inflatable endoscopic prosthesis (Bettocchi, 2010). In Peyronie's disease, men may experience penile deformity due to bending, which can negatively affect erectile function. In these cases, surgery focuses on correcting the curved shape of the penis and may involve removing the problematic tissue (Tunugutla, 2001). Penile elongation may also be performed, although is not very common, and is mainly indicated in cases of microphallia (Campbell et al., 2017)

Regarding the psychological approach, Psychotherapy and counseling can help in the development of communication and stress management skills, as well as strengthening a couples' relationship (Hofmann, 2012). Most frequently Cognitive behavioral therapy (CBT) is used, which focuses on identifying and addressing the thoughts and feelings associated with premature ejaculation and sexual dysfunction in general. Patients learn ejaculation control techniques and how to deal with stress related to sexual activity (Althof, 2014). Also, behavioral approaches such as "Start-Stop" and "Squeeze" techniques can help control ejaculation. In the "Start-Stop" technique the man withdraws from the sexual act before ejaculation and then starts again. In the "Squeeze" technique, the man applies pressure to the base of the penis to delay ejaculation (Athanasiadis, 2002).

Treatment of infertility

Treatment of the underlying cause with the ultimate goal being conception. If the cause is due to hormonal disturbances of the hypothalamus-pituitary-gonadal axis, hormone replacement therapy is used. Specifically, some ongoing studies suggest that GnRH (gonadotropin releasing hormone) may be administered subcutaneously with pump in a pulsatile manner, in cases of hypogonadotropic hypogonadism. Its effect is that it induces spermatogenesis by promoting the release of gonadotropins. Gonadotropins themselves, such as recombinant FSH, recombinant LH and recombinant hCG may be used when there is pituitary insufficiency. Dopamine agonists, such as Bromocriptine and Cabergoline are effective in the treatment of hyperprolactinemia caused mainly by tumors in the pituitary gland. In this case if medicational approach is ineffective, surgery for tumor removal is performed.(Dabaja,2014). Moreover, commonly used aromatase inhibitors, such as Letrozole, aid fertility by promoting testosterone production and inhibiting estradiol levels via suppression of aromatase, which is responsible for testosterone conversion to estradiol (Yang, 2022). Another hormonal treatment that enhances testosterone production is the selective estrogen receptor modulators, namely Tamoxifen Citrate and Clomiphene Citrate. Both act antagonistically on the estrogen receptors placed in the hypothalamus and pituitary gland, suppressing the negative feedback of estrogen on the hypothalamus-pituitary-gonadal axis. (Foran, 2023).

The surgical approach on treatment of male infertility involves restoration of the anatomical abnormalities leading to impaired fertility. Microsurgical varicocelectomy is widely used in cases of varicocele (Mehta, 2013). Other repair methods of the genitourinary vasculature include vasovasostomy and vasoepididymostomy, which are effective in men with obstructive azoospermia. Vasovasostomy is

performed in men with previous vasectomy (Herrel,2013), whereas vasoepididymostomy also in those with epididymal infections (Chen, 2016).

In terms of Assisting Reproductive Techniques (ART), intrauterine insemination (IUI) can be used in some cases of infertility, such as in mild male fertility disorders, involving reduced sperm count and motility, in anovulation of the female partner and in cases of hostile cervical mucus (Cohlen et al., 2018). IUI is performed in combination with administration of medications for ovarian stimulation (OS). Such drugs are gonadotrophins (rec-FSH, rec-LH, rec-hCG), aromatase inhibitors (Letrozole) and selective estrogen receptor modulators (Clomiphene Citrate). Studies have shown that IUI-OS highly increase the chances of conception and live births especially in cases of unexplained infertility (Wessel, 2022). Another technique commonly used for infertile couples is in vitro fertilization (IVF). During IVF, mature oocytes are collected and combined with spermatozoa in culture media. (Parish, 2016) Ovarian stimulation prior may be required but it isn't always necessary (Jain,2023). Lastly, intracytoplasmic sperm injection (ICSI) directly to the cytoplasm of the oocyte can be performed in cases where there's history of fertilization failure with IVF (Van der Westerlaken, 2005).

Results

Sexual dysfunction and male infertility are two important topics in the field of human reproduction and sexual health. Many factors, such as chronic diseases, hormonal disturbances, anatomical or genetic disorders, infectious diseases, psychological issues and more, may lead to both of them. Although they are separate entities in theory, as the first is associated with problems occurring during the sexual act, and the last one refers to the reproductive capacity of males, they often intertwine with one another. The

percentage of infertile men facing sexual dysfunction is estimated according to studies of the last 15 years to be around 17,8% to 61,6% (Liu, 2022). Studies have shown that sexual dysfunction itself can lead to infertility, as it can create stress and anxiety, which in some cases can affect sexual performance. This is more prevalent in infertile couples undergoing IVF and other assisting reproductive techniques. Failure to conceive promotes anxiety and depression in both participants, impairing sexual function. To address in depth and adequately this interconnected issue, counseling and medical intervention may be necessary. Recognizing and treating sexual dysfunction can help increase chances of conception, enhance male fertility and improve sexual performance. (Brennan, 2007)(Capogrosso, 2021) (Fernández-Zapata, 2023).

Conclusion

Sexual dysfunction and male infertility are both significant and complex subjects in the ongoing field of reproductive medicine, which are caused by a variety of factors, either physical and/or psychological. Scientific research has shown that early diagnosis and treatment of these problems with psychotherapy, drug therapy and/or surgery according to the cause, are of utmost importance for the quality of life of the men themselves and their perspective partners.

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