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A Review of Infertility, Lifestyle, and Physical Activity

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Abstract

Infertility is a health problem that affects about 10-15% of couples worldwide. Infertility is defined as the inability of couples to successfully conceive a child after one year of unprotected sex. The causes of infertility are often not easily identified. However, this disorder appears to be due to genetic or environmental factors, some of which may be modifiable and may be considered as a treatment option. The use of emerging infertility treatment technologies has been somewhat effective. However, these methods are very expensive and, in some cases, their success rate is relatively low. A sedentary lifestyle can lead to several disorders such as cardiovascular diseases, diabetes, cancer and conditions such as obesity. Obesity can have a negative effect on the fertility of couples. Overall, it seems that changing the sedentary lifestyle and increasing physical activity by performing regular exercise training can enhance the chances of fertility. However, it should be noted that strenuous exercise training has a negative effect on fertility.

Keywords: Infertility, Lifestyle, Physical Activity, Obesity

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INTRODUCTION

Infertility is one of the most serious problems facing many couples. Infertility is defined as the inability of couples to achieve a successful pregnancy after one year of regular unprotected intercourse. There are two types of infertility: primary infertility refers to couples who have not experienced pregnancy after 12 months of intercourse without taking birth control measures, while secondary infertility refers to couples who have previously experienced pregnancy (Nascimento & Vilasboas, 2013). Diagnosis of a disease or condition leading to infertility followed by treatment with surgery, medication, in vitro fertilization (IVF) or other assisted reproductive technologies (ART) do not always lead to successful pregnancy and live birth. For instance, although more than 70,500 treatments with ART were recorded in Australia and New Zealand in 2009, only 17.2% of cases experienced live birth (Nascimento & Vilasboas, 2013).

In addition, ART therapy is very expensive for both the government and the patients. Despite the low probability of success, alternative therapies such as traditional medicine offer less invasive and cheaper physical and mental therapies. One of the factors attributed to infertility is a sedentary lifestyle, which is also associated with many other disorders such as cardiovascular disease, diabetes, and cancer. Studies have shown that obesity and a sedentary lifestyle can negatively affect the fertility of couples. Therefore, it seems that making lifestyle changes and especially increased physical activity by performing regular exercise training can be effective in improving the fertility of couples. Therefore, in the following sections, we will discuss the relationship between infertility, lifestyle and physical activitys.

DISCUSSION

Male infertility

Male infertility has been attributed to several factors, such as infection, injury, exposure to toxins, anatomical abnormalities, chromosomal abnormalities, systemic diseases, and sperm antibodies. Other potential risk factors include smoking, alcohol consumption, obesity, and aging. Assessing male fertility begins with a review of the patient's background and his physical condition, with a focus on previous fertility, pelvic or scrotum surgeries, environmental diseases, and exposure to toxins.

Laboratory evaluation is also performed through semen analysis. For collecting sperm samples, ejaculation should be avoided for 48 to 72 hours prior to sampling. Since sperm production takes more than two months, it is recommended to wait for three months before repeating the process of sampling (National Collaborating Centre, 2013). After sample analysis, the presence of oligospermia or azoospermia could be indicative of hypogonadism. Taking morning testosterone (normal: 240-950 ng/dL) and follicle-stimulating hormone (normal: 1.5-12.4 IU/ml) levels can be useful in the differentiation of primary and secondary disorders. Decreased testosterone levels along with increased FSH levels are indicative of hypogonadism as a major factor. Increased testosterone levels along with decreased FSH levels are indicative of a secondary cause. Some factors, including hyperprolactinemia, can be reversed with proper treatment. Other possible tests needed include testicular biopsy, genetic testing, and imaging (Lindsay & Vitrikas, 2015).

Female infertility

Causes of female infertility include ovulation disorders, uterine problems, failure in fallopian tubes, and peritoneal factors. While cervical factors are also thought to be involved in female infertility, they are rarely the sole factor. Evaluation of cervical mucosa is unreliable; therefore, its evaluation alone does not help in the treatment of infertility (Practice Committee, 2012). Initial background check of the patients should include the status of menstrual cycle, timing and frequency of sexual intercourse, contraceptive history, previous pregnancies and outcomes, pelvic infections, medications, occupational status, drug and alcohol use, smoking, and previous surgeries of reproductive organs. An assessment of the endocrine status and the health of reproductive organs should be performed. Other considerations include vaccination against preventable diseases, such as rubella and chickenpox, sexually transmitted infections, and cervical cancer (Lindsay & Vitrikas, 2015). The World Health Organization (WHO) categorizes the disorders associated with ovulation into three groups based on hypothalamic-pituitary insufficiencies (10%) (Group 1), disorders of the hypothalamic-pituitary-ovarian axis (85%) (Group 2), and ovarian failure (5%) (Group III). Women in group I are usually suffering from amenorrhea and have low gonadotropin levels, often due to strenuous exercise training or low weight. Women in group II are those with polycystic ovary syndrome

(PCOS) and hyperprolactinemia, while women in group III can only be fertilized by in vitro fertilization and receiving eggs from donors (Lindsay & Vitrikas, 2015). Apparently, women with regular menstrual cycles have the ability to ovulate and to confirm ovulation, serum progesterone levels should be measured on day 21 of menstrual cycle. In case of an irregular menstrual cycle, testing should start seven days before the possible date of menstruation and be repeated weekly until menstruation. Progesterone levels of 5 ng/ml or more are indicative of ovulation. In women with no ovulation, more tests should be performed to determine the treatable causes, such as thyroid disorders or hyperprolactinemia. High levels of serum FSH (30-40 IU/L) combined with low levels of estradiol can discriminate ovarian failure from hypothalamic-pituitary insufficiencies, in which usually low or normal FSH (10 IU/L) and low estradiol levels are present (Practice Committee, 2012).

Basal body temperature is no longer considered as a reliable indicator of ovulation and is not recommended for ovulation assessments (National Collaborating Centre, 2013). High levels of FSH (10-20 IU/L) on the third day of the menstrual cycle are associated with infertility. High levels of serum estradiol (over 60 to 80 pg/ml) together with normal levels of FSH are also associated with reduced pregnancy rates. These laboratory results may be suggestive of ovarian failure or diminished ovarian reserve (Nelson, 2009). Other tests for assessing ovarian reserve, including the clomiphene citrate challenge test, antral follicle count, and antimullerian hormone levels, are also commonly used to predict the ovarian response to exogenous gonadotropins and ART. Nevertheless, despite the widespread use of these tests, their predictive value ranges from weak to moderate (Broekmans et al, 2006).

Lifestyle and infertility

With the advent of ART, many of the problems associated with infertility have been resolved, and in advanced countries, most couples are willing to use this technology. However, this technology, with the success rate of <37% for men aged 35 years, 16% for women aged 40 years, and 2% for women age >43 years imposes a great economic cost on the public health sector (Chavarro et al, 2007). Therefore, important factors, such as lifestyle, which can affect public health and fertility need more investigation. Healthy lifestyle is defined by the WHO as a set of

behaviors that provides physical and mental health in humans. Nutrition, physical activity, and sleep, comprise the physical aspects of life while social relationships, coping with stress, research and learning, and moods constitute the mental aspect (Wise et al, 2011). Nowadays, sedentary lifestyle and inadequate physical activity have led to many health problems for humans. A sedentary lifestyle is considered as a condition in which the energy required for activities is less than 1.5 MET (like sitting or lying down). Inadequate physical activity has been defined as insufficient physical activity in daily life (i.e., less than 150 minutes of moderate-intensity exercise training per week) (Hamburg et al, 2007). These two conditions sometimes coexist and sometimes do not. In fact, one may have a sedentary lifestyle while having sufficient physical activity. Under these conditions, physical activity can alleviate the harmful effects of a sedentary lifestyle. However, it cannot totally eliminate those (Biswas et al, 2015). Sedentary lifestyle and inadequate physical activity have been shown to separately affect several health-related factors, non-communicable diseases and mortality (Foucaut et al, 2019). Lifestyle is defined according to several specific behavioral patterns that result from the interaction between personality traits, social relationships, environmental conditions, and socioeconomic status. McDonald and Thomson consider nutrition, exercise, personal care, smoking, alcohol and drug use, social relationships, and stress management as the constituents of lifestyle (Evenson et al, 2014). Modern life has intensified several specific factors related to lifestyle. For instance, obesity caused by inactivity and/or an unbalanced diet can upset the hormonal balance (Gudmundsdottir et al, 2009). Obesity is associated with a sedentary lifestyle and inadequate physical activity. Obesity and being overweight affect the fertility of couples. Numerous studies have shown that body mass index (BMI) above 25 is associated with infertility in both men and women (Ramlau et al, 2007; Hammoud et al, 2008; Jungheim et al, 2008). Obesity is associated with decreased semen quality, decreased sperm concentration and motility, sperm DNA damage, poor egg quality, as well as impaired ovulation and implantation (Foucaut et al, 2019). Idiopathic or unexplained infertility which affects 30-40% of infertile couples is defined as the absence of recognizable symptoms in couples who have not had children after one or two years of unprotected intercourse. The standard protocols for research on

idiopathic infertility include ovulation testing, fallopian tube occlusion, and semen analysis. Diagnosis of idiopathic infertility can be very frustrating and annoying for couples and treatment is often unscientific (Ray et al, 2012).

Even if a reason is not specified, changing living conditions and lifestyle can be effective for the treatment of idiopathic infertility. As a result, it is important to focus on the modifiable factors in the lifestyle of these patients (Foucaut et al, 2019).

Physical activity and female fertility

It is well established that physical activity and exercise are associated with a reduced risk of many disorders. It has been suggested that women with physical activity not only avoid disorders such as cardiovascular diseases, type 2 diabetes, and breast and colon cancer, but also gain less weight during pregnancy. These conditions are associated with a reduced risk of gestational diabetes and postpartum depression (2018 Physical Activity Guidelines, 2018). Recent studies have shown that the rate of women with a BMI within the range of overweight and obesity is increasing (Dobson et al, 2012). This is of great concern as reproductive disorders such as infertility are more prevalent in overweight and obese women (Da˘gZÖ,Dilbaz, 2015). On the other hand, a study on female athletes showed that high levels of high-intensity physical activity can be associated with menstrual irregularities and increased possibility of infertility (Gabriela et al, 2019).

High-intensity exercise training can disrupt ovulation and according to previous studies, strenuous activities can increase fertility problems by up to 2.3 times (Gudmundsdottir et al, 2009). However, these results are not consistent in all studies. The reason for discrepancies in results could be attributed to differences between the definition of high-intensity exercise, diet control or weight loss programs used in conjunction with exercise and the duration of exercise (Hakimi & Cameron, 2017). High-intensity exercise training seems to disrupt ovulation by inducing chronic energy deficiency. Chronic energy deficiency is one of the most important mechanisms attributed to ovulation disorders and reportedly, controlling the balance between energy intake and the energy consumed during exercise can solve hormonal disorders involved in ovulation problems (Loucks & Callister, 1993). On the other hand, other studies have shown that anovulation is often associated with the lack of available

energy (De Souza et al, 1998). In addition, according to previous studies, the suppression of ovulation is commonly associated with a variety of stresses, and any type of stress in the reproductive age can cause infertility as the hypothalamic-gonadal axis is highly sensitive to available energy and other types of stress (Power & Schulkin, 2008; Howlett et al, 1984).

On the other hand, these fertility problems seem to be in part due to the complex interaction of neuro-hormonal mechanisms resulting from strenuous activities. During strenuous exercise, temporary increase in ovarian hormone levels and disruption of hypothalamic regulatory pathways reduce the circulating estradiol levels and ovarian stimulation. These changes are particularly noticed in case of negative energy balance, which is observed in many female athletes. However, often, especially in upper middle and high- income countries, many young women have a positive energy balance and do not exercise frequently (Gabriela et al, 2019). In non-athletes, most studies on physical activity and fertility have focused on overweight and obese women with ovarian disorders such as PCOS. Studies on diet and exercise in women with PCOS have shown that exercise reduces insulin resistance and restores ovulation. The proposed mechanism by which physical activity and exercise restore ovulation begins with increased insulin sensitivity, leading to steroid production at normal levels (Hakimi & Cameron, 2017).

Gonadotropins or clomiphene (as an ovulation stimulant, which stimulates the pituitary gland to secrete gonadotropins) are commonly used for the treatment of infertility, Research on women with PCOS has shown that exercise is also effective as it has the potential to recycle the GnRH cycle, resulting in spontaneous ovulation (Froment & Touraine, 2006). Systematic studies have also shown that exercise with or without a diet plan can restore ovulation in overweight or obese patients with PCOS by modulating the hypothalamic-pituitary-gonadal axis (Hakimi & Cameron, 2017). Several studies have shown that in order for exercise to have a positive effect on fertility and live birth, it should not necessarily lead to weight loss (Gabriela et al, 2019; Best et al, 2017). Previous studies have shown that high BMI and obesity are associated with primary infertility, and weight loss in overweight and obese women is an effective way to improve fertility and pregnancy (Da˘gZÖ,Dilbaz,

2015). Also, a systematic study showed that weight loss following diet plans and exercise is linked with an increased chance of pregnancy, improved ovulation and improved menstrual regularity (Best et al, 2017).

However, while weight loss appears to play a significant role in improving fertility, studies show that physical activity in women with PCOS can be effective in restoring fertility even in the absence of a significant weight loss (Harrison et al, 2010). By studying the effect of exercise on female fertility, Aria et al (2020) reported that exercise, irrespective of BMI change, has a positive effect on improving female fertility. Evidence also suggest that physical activity improves ovarian reserve markers regardless of weight (Surekha et al, 2014).

Therefore, weight loss may be a mediator of any association between physical activity and reproductive health; however, it is difficult to distinguish the benefits of physical activity from those of weight loss in fertility. In general, there seems to be an inverse U relationship between exercise, BMI, and ovulation, indicating that women with sedentary lifestyle and high BMI as well as women with physical activity and low BMI are more prone to hormonal disorders and menstrual irregularities (Hakimi & Cameron, 2017).

Physical activity and male infertility

Some studies have reported limited benefits for an active lifestyle. In a study, Vaamonde et al (2009) examined 16 active and 15 sedentary men. Although their activity rates were based on their own claims, the validity of the data was improved by assessing maximal oxygen uptake of the participants, according to which the mean oxygen uptake of sedentary and active subjects was 36.9 and 51.1 mL/min/kg, respectively. Although their findings showed no difference in testosterone concentrations, active men showed a normal sperm morphology as well as higher FSH and total testosterone levels. These initial data were not consistently confirmed by studies with more participants. A cross-sectional study on 215 healthy men, who were categorized based on their physical activity, showed different semen parameters when cases with the lowest (<three hours) and highest (>nine and a half hours) physical activity levels were compared (Minguez-Alarcon et al, 2014).

Gaskins et al (2014) showed slight differences between men with varying levels of physical activity. They selected 213 men at a fertility clinic and subjects were asked to complete a questionnaire about their

exercise habits. When patients with the lowest and highest levels of physical activity were compared, a statistically significant improvement was observed in the sperm concentration of subjects participating in strength training programs or outdoor activities. Gaskins et al (2015) studied the effect of watching television, possibly as a better indicator of a sedentary lifestyle, on semen quality in healthy young men. Among the 189 participants, those who spent the most time watching television (>20 hours per week) showed a 44% lower sperm concentration than those who did not watch television during the week. In one of the most extensive studies in this field, Eisenberg et al (2015) examined fertility problems associated with difficulty of physical activity in workplace in 456 men. They found that testosterone levels were negatively affected by increased work difficulty. Men whose jobs required heavy physical activity showed higher oligospermia compared to other subjects. Based on the current findings, there is an obvious complex relationship between reproductive health and physical activity. Notably, mild to moderate-intensity physical activity seem to positively affect fertility, while strenuous physical activity or jobs requiring heavy physical activity have a negative effect on fertility (Hayden et al, 2018). Studies have shown that strenuous exercise interferes with male fertility and its exact mechanism possibly involves a variety of factors, one of which could be the down-regulation of gonadotropins and sex hormones.

In one of the first studies in this area, it has been shown that high-intensity exercise training has a negative effect on semen parameters (Vaamonde et al 2009). In another study, endurance athletes were evaluated and similar results were obtained (Griffith et al, 1990). On the other hand, several other studies considered the effect of exercise on the hypothalamic–pituitary–gonadal axis. Steinacker et al. surveyed ten rowers during preparation for the World Championships. Analysis of their blood samples showed decreased levels of FSH, LH and total testosterone (Steinacker et al, 2000). Contrary to these findings, different results were obtained when men were exposed to moderate-intensity physical activity. Grandys et al. surveyed 15 cyclists during their training. In their study, total testosterone levels increased for about 543-635 ng/dL, while sex hormone-binding globulin levels decreased (Grandys et al, 2009). The increased testosterone levels in the testicles and the improved sperm production seem rational. Of note, Wise et al.

suggested that strenuous bicycling interferes with sperm production. In their study, sperm samples were taken from 2261 men and subjects were asked to complete a questionnaire about their physical activity. According to their results, bicycling for more than 5 hours per week was associated with lower sperm count and quality (Wise et al, 2011). Safarinejad et al. examined 286 subjects randomly assigned to high-intensity exercise and moderate-intensity exercise. In their study, gonadotropins and semen were analyzed. The testosterone concentration of men who participated in high-intensity exercise increased from 66.2 million to 35.4 million per milliliter. Sperm motility, LH, FSH, and total testosterone also decreased significantly. Decreasing trends in these parameters were also seen in those exercising with moderate-intensity, however, only the reduction in sperm concentration was statistically significant (Safarinejad et al, 2009). Consistent with these findings, men who participated in strenuous exercise showed sperm DNA damage (Vaamonde et al, 2017).

The above studies suggest that strenuous exercise has a negative effect on male fertility. Considering the results of these studies, it can be concluded that men who want to be fertile should not do strenuous exercise (Hayden et al, 2018).

CONCLUSIONS

Moderate-intensity physical activity and exercise seem to have a positive effect on increasing the chances of fertility in men and women, while high-intensity exercise training can reduce the chances of fertility in couples. On the other hand, in order for physical activity and exercise to have a positive effect on fertility, one should not expect weight loss, as these positive effects can occur regardless of weight loss and BMI change.

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