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Sleep Disorders and Reproductive Health: Mechanisms, Consequences, and Potential Interventions

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Abstract

Introduction

The role of sleep in maintaining the body's homeostasis has been the subject of an increasing number of scientific studies, with reproductive health also being dependent on it. Reduced fertility, resulting from the deterioration of reproductive cell quality due to hormonal imbalances, may be a consequence of sleep deprivation. Chronic stress, obesity, and other factors accompanying sleep disturbances can impair the functioning of hormonal axes, ultimately leading to oxidative stress—a metabolic basis for fertility issues. The aim of this study is to analyze the impact of sleep disorders on reproductive health, focusing on the mechanisms, clinical consequences, and potential therapeutic interventions.

Materials and Methods

This article is based on an analysis of scientific literature concerning the impact of sleep disturbances on reproductive health, utilizing data from databases such as PubMed, Frontiers, and Google Scholar. Studies in fields such as endocrinology, sleep medicine, gynecology, andrology, and psychology were included. Both primary research and systematic reviews, as well as meta-analyses with high methodological quality and statistical significance, were analyzed. This approach provides a comprehensive overview of the relationship between sleep and fertility, considering both biological and psychological mechanisms.

Conclusions

In both sexes, sleep disturbances can lead to reproductive health problems due to hormonal imbalances, resulting in the deterioration of reproductive cell quality. Factors such as obesity, stress, or shift work further increase the risk of infertility. Recent findings emphasize that mindfulness techniques, cognitive-behavioral therapy, improved sleep hygiene, and even melatonin supplementation may contribute to the success of infertility treatments, including assisted reproductive techniques. It is crucial to raise public awareness about the role of sleep and stress in fertility issues. However, further research is needed to better understand these relationships and develop personalized therapies.

Keywords: insomnia, reproductive health, hormonal disorders, shift work, sleep hygiene

INTRODUCTION

Numerous biological processes, such as immune responses, cell regeneration, and hormonal regulation, depend on sleep, which is essential for maintaining the body's homeostasis. The significance of sleep for reproductive health, in both women and men, is increasingly recognized, with a growing body of research dedicated to this topic. Insomnia, circadian rhythm disturbances, sleep deprivation, and other issues within the spectrum of sleep disorders may underlie hormonal dysfunctions, reduced quality of reproductive cells, and impaired reproductive abilities [1,2]. Irregular menstrual cycles in women, reduced semen parameters in men, and even fertility challenges such as failures in assisted reproductive procedures, including in vitro fertilization (IVF), have been linked to inadequate sleep, as documented in scientific literature [3,4].

The mechanisms underlying the relationship between sleep quality and fertility involve hormonal changes as well as the negative effects of oxidative stress. The combination of sleep disturbances with other significant infertility risk factors, such as obesity or chronic stress, is particularly detrimental to reproductive health [5,6,7,8].

The aim of this paper is to provide a comprehensive discussion of the impact of sleep disturbances on reproductive health, with a focus on biological and psychological mechanisms, clinical consequences, and potential therapeutic interventions. Recent studies on the relationship between sleep and fertility will be presented, along with recommendations for improving sleep quality as a supportive element in infertility treatment.

MATERIALS AND METHODS FOR INFORMATION SEARCH IN THE ARTICLE

The article is based on an extensive analysis of scientific literature regarding the relationship between sleep disorders and reproductive health. The cited studies were sourced from scientific databases such as PubMed, Frontiers, Google Scholar, and other academic platforms that include research on sleep, fertility, and reproductive health. Data from various fields, including endocrinology, sleep medicine, gynecology, andrology, and psychology, were analyzed to provide a comprehensive overview of the topic.

The article discusses both primary research, which directly measures the impact of sleep disorders on reproductive health, and systematic reviews and meta-analyses. The studies included are characterized by high methodological quality and statistical significance concerning the effects of sleep on the reproductive system. This approach allows for a detailed and reliable depiction of the relationship between sleep disorders and reproductive capabilities, considering both biological and psychological mechanisms.

SLEEP DISORDERS AND WOMEN'S REPRODUCTIVE HEALTH

Key hormonal and physiological processes essential for women's reproductive health are regulated by sleep. A meta-analysis conducted by Caetano MD and colleagues demonstrated that women who slept less than 5 hours per night were more likely to experience irregular menstrual cycles compared to those sleeping over 8 hours. Furthermore, a study on 287 nurses revealed that menstrual cycle irregularities occurred twice as often in those suffering from insomnia [9,10].

The levels of hormones crucial for the reproductive system, such as TSH, progesterone, estrogen, and prolactin, are also regulated during sleep, and sleep deprivation leads to hormonal imbalances. Acute sleep deprivation significantly increases TSH levels, which can result in anovulation, miscarriages, and menstrual irregularities,

including amenorrhea [2]. Prolactin, a hormone produced by the pituitary gland that stimulates lactation, plays a vital role in human reproductive health. Prolactin is secreted during sleep; therefore, women with narcolepsy (regardless of sleep apnea presence) exhibit reduced prolactin levels. Sleep disturbances can disrupt prolactin secretion, although this correlation is ambiguously described in the literature. Even brief awakenings suppress prolactin secretion, as its levels significantly rise after falling asleep, peaking at night. Sleep deprivation can lead to hyperprolactinemia, which in turn causes anovulation associated with polycystic ovary syndrome (PCOS) and may correlate with endometriosis. While the effect of sleep on progesterone levels is not yet fully understood, low progesterone levels may increase the risk of sleep-disordered breathing in women with PCOS [2,11].

Estradiol, the primary estrogen during the reproductive period, is critical for ovulation and follicular development due to its regulation of FSH and LH. Estradiol, FSH, and LH interact through feedback loops to ensure ovulation occurs. Even partial sleep deprivation in women of reproductive age led to an increase in estradiol levels. In women, a regular circadian rhythm was associated with lower estradiol levels compared to those with an irregular sleep schedule. Additionally, estradiol levels decreased by 60% in women with regular sleep schedules compared to those with irregular rhythms. Poor sleep quality is also associated with high estradiol levels. Interestingly, estrogen therapy improved sleep quality in women with sleep-disordered breathing.

The regularity of the human circadian rhythm plays a crucial role in maintaining women's fertility at different ages. Women's reproductive health is also linked to endogenous melatonin secretion and its suppression due to bright light exposure. Studies have shown that lower melatonin concentrations in follicular fluid correlate with higher levels of reactive oxygen species (ROS) and reduced oocyte quality in infertile women. Sleep deprivation reduces endogenous melatonin secretion, lowering its levels in follicles and increasing their susceptibility to the adverse effects of oxidative stress [2,12].

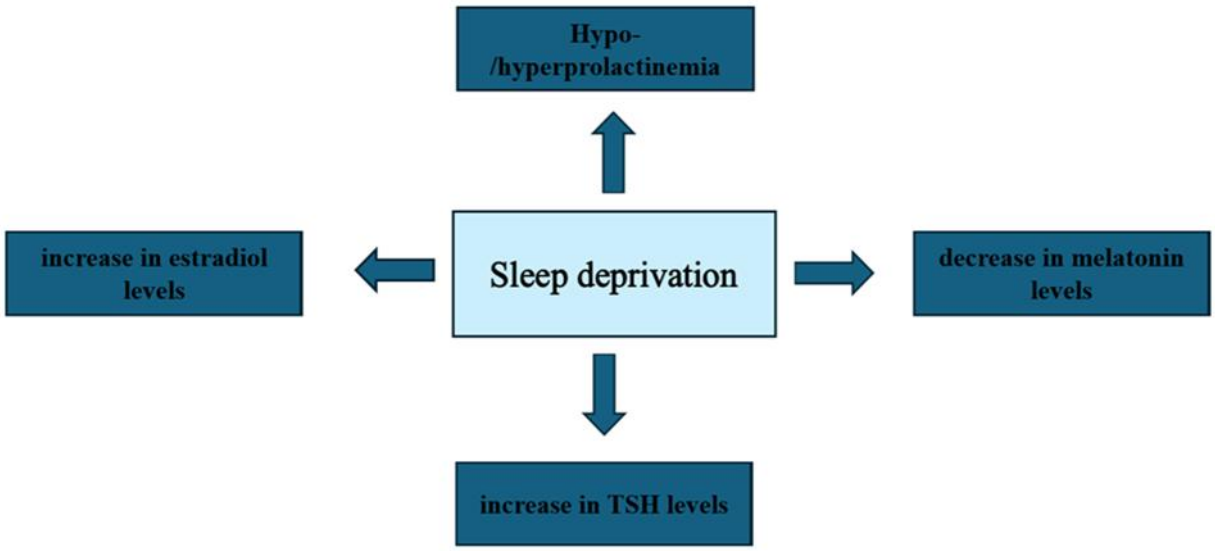

Figure 1. The Impact of Sleep Disorders on Hormone Levels.

SLEEP DISORDERS AND MEN'S REPRODUCTIVE HEALTH

Studies conducted on both humans and animal models have shown that insufficient sleep among adult men negatively affects the functioning of their reproductive system [1,13]. A meta-analysis by Zhong et al. revealed that teratozoospermia (where <4% of sperm in semen are morphologically normal), oligospermia (reduced total sperm count in ejaculate), and decreased progressive motility of sperm are associated with sleep disorders [1]. Additionally, obstructive sleep apnea (OSA) in men can affect semen quality, as Leydig cells in the testes, responsible for testosterone production, are sensitive to hypoxia caused by breathing disturbances in this condition. Men with OSA have been observed to have reduced sperm counts, decreased motility, and higher levels of sperm DNA fragmentation, increasing the risk of fertilization issues [1,14]. Elevated corticosteroid levels, released in response to stress caused by sleep deprivation, further impact the activity of the hypothalamic-pituitary-gonadal (HPG) axis by suppressing it, leading to decreased testosterone production [2,15]. The functioning of male gonads is regulated by various substances, such as neurotransmitters and neuropeptides, including serotonin (5-HT), which is naturally present in Leydig cells. Animal studies have shown that serotonin levels increase in the body as a result of sleep deprivation (SD). It has also been demonstrated that serotonin inhibits testosterone production, leading to reduced testosterone levels due to sleep deprivation [2]. Leprout and his team investigated the impact of one week of sleep restriction on testosterone levels in young, healthy men. Although the sample size was small (28 participants), and the participants slept 5 hours per night for a week, this reduction led to a 10%-15% decrease in daily testosterone levels. Such chronic fatigue

conditions affect at least 15% of the U.S. working population. For comparison, the natural aging process decreases testosterone levels by approximately 1%-2% per year [16]. Low testosterone levels result in decreased libido and erectile dysfunction, negatively impacting male reproductive potential [17]. Another hormone playing a significant role in the male reproductive system is melatonin. It is essential because it regulates other hormones crucial for reproductive physiology, such as gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH). Insufficient melatonin levels can disrupt their secretion, leading to hormonal imbalances. Furthermore, melatonin protects the genetic material in sperm from oxidative stress, contributing to their quality. A melatonin deficiency may weaken this protection, adversely affecting reproductive capacity [18].

Chronic insomnia, as is well known, affects mental health, increasing the risk of depression and anxiety, which may indirectly contribute to reduced sexual function and procreative ability [19].

SLEEP DISORDERS AND COUPLES' FERTILITY

As mentioned earlier, sleep plays a crucial role in maintaining the proper function of the hypothalamic-pituitary-ovarian axis in women. Sleep problems can cause hormonal imbalances, such as reduced levels of gonadotropins (FSH, LH), which affect ovulation. In men, insufficient sleep negatively impacts testosterone levels, potentially leading to reduced semen quality, including lower sperm count, decreased motility, and abnormal morphology [1, 2, 16]. Moreover, metabolic disorders such as insulin resistance and other hormonal imbalances leading to obesity can also be caused by insufficient sleep. This occurs because lack of sleep reduces cellular sensitivity to insulin, leading to elevated blood glucose levels and promoting fat storage. The levels of appetite-regulating hormones such as leptin and ghrelin are also modulated during sleep. Leptin, responsible for suppressing hunger, decreases with sleep deprivation, while ghrelin, which stimulates hunger centers in the hypothalamus, is elevated. As is well-known, obesity in adults is often the result of fast-paced lifestyles with insufficient sleep, leading to excessive calorie intake, particularly of highly processed, carbohydrate-rich foods [5, 20]. Obesity is a significant risk factor for infertility in both women and men. The mechanisms through which it impacts the reproductive system are complex and multifactorial. Elevated serum leptin levels result from increased fat tissue, which produces leptin. Leptin affects female gonads, including the ovaries and the endometrium, by inhibiting steroidogenesis in granulosa and theca cells. This leads to abnormalities in the growth of dominant follicles and oocyte maturation and negatively impacts the endometrium's ability to implant an embryo. Central nervous system leptin

resistance decreases GnRH pulse secretion, while excess leptin also promotes peripheral insulin resistance. Fat tissue acts as an endocrine organ; its growth in the abdominal area is associated with increased estrogen (E2, E1) and androgen levels, as well as their storage. This reduces the availability of sex hormone-binding globulin (SHBG), increasing the bioavailability of estrogens and androgens in target tissues. Excess androgens in the ovaries can lead to follicular atresia, resulting in anovulatory cycles. Hyperestrogenism reduces endometrial receptivity, contributing to infertility. Hyperandrogenism, hyperleptinemia, elevated free fatty acids (FFAs), and cytokines (e.g., IL-6, TNF-α) exacerbate insulin resistance. In response to hyperinsulinemia, ovaries produce more androgens, causing follicular atresia and ovulatory dysfunction. Additionally, elevated insulin levels and FFAs, combined with dysregulation of the GHRH, somatostatin, and ghrelin axes, lower growth hormone (GH) levels, potentially impairing ovarian and endometrial function. Excess FFAs in the ovaries are linked to mitochondrial dysfunction in oocytes, endoplasmic reticulum stress, apoptosis of cumulus-oocyte complexes, and delayed meiotic maturation, increasing the risk of aneuploidy and oocyte death. Insulin resistance disrupts endometrial decidualization, impairing blastocyst implantation. As a result, obesity leads to difficulties in conception, higher miscarriage rates, and pregnancy complications, reducing live birth rates in both natural and assisted reproduction [6, 7].

The impact of obesity on male fertility is less well understood than in women. However, elevated BMI is associated with reduced SHBG levels and testosterone, alongside increased estrogen levels. These hormonal changes, including decreased testosterone and increased estrogen, are long associated with infertility and reduced sperm count due to disruption of the hypothalamic-pituitary-gonadal (HPG) axis. The FSH/LH ratio, inhibin B, and SHBG levels, which regulate Sertoli cell function and spermatogenesis, are lower in obese men. Dysfunction in FSH receptor signaling leads to gametogenesis abnormalities and hormonal imbalance. Obesity in men is linked to lower total and free testosterone levels, with hypogonadotropic hypogonadism being a primary cause. Increased estrone and estradiol levels, resulting from enhanced peripheral aromatization of androgens, negatively affect GnRH secretion, suppressing FSH and LH production. Inflammatory cytokines like TNF-α and IL-6, elevated in obese individuals with type 2 diabetes, impair the HPG axis, resulting in secondary hypogonadism, often associated with insulin resistance. SHBG levels decrease due to hyperinsulinemia typical of obesity-related insulin resistance. Interestingly, increased scrotal fat can elevate local temperature, negatively affecting semen parameters by causing

DNA fragmentation, oxidative stress, and reduced sperm motility. Additionally, leptin, primarily produced by fat cells, can damage sperm or cells involved in spermatogenesis. High leptin levels, common in obese men, inhibit testosterone production in Leydig cells, impairing the HPG axis and reducing testosterone synthesis. Leptin resistance also contributes to hormonal imbalance and reproductive dysfunction [8].

Another important area of research is the impact of partners' sleep quality on in vitro fertilization (IVF) success. In a study by Marco Reschini, the relationship between women's sleep quality and IVF outcomes was analyzed. Among 263 women undergoing oocyte retrieval, sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), where scores >5 indicated poor sleep quality. Women with confirmed clinical pregnancies (31%, 81 women) had significantly lower PSQI scores (median 4 [3–5]) compared to those without successful pregnancies (median 5 [3–7]). Better sleep quality, as reflected by lower PSQI scores, was associated with higher chances of IVF success. Women with PSQI scores >5 had approximately 50% lower odds of pregnancy compared to those with good sleep quality (adjusted OR 0.50, $p = 0.03$). These findings suggest that improving sleep quality could enhance IVF outcomes [3]. Similarly, Cong-Qi Du and colleagues observed that men with poorer sleep quality had lower sperm counts, reduced motility, and a lower percentage of morphologically normal sperm compared to well-rested men. These findings are particularly significant for procedures like intrauterine insemination (IUI) or intracytoplasmic sperm injection (ICSI) [4].

Mental health significantly impacts sleep quality. Previous in vivo studies have shown a direct relationship between stress hormones and IVF success. For example, An et al. observed that lower serum cortisol and norepinephrine levels were associated with higher pregnancy rates. Urinary norepinephrine levels during embryo transfer also showed similar trends. Chronic inflammation may also influence IVF success. Women with stress-laden lifestyles showed elevated cervical-vaginal cytokine levels (e.g., IL-6 and IL-1β), which are associated with the innate immune response. Dysregulation of inflammatory response due to glucocorticoid receptor resistance has been identified as a risk factor for adverse pregnancy outcomes, including preterm birth [3, 21, 22].

Stress affects sleep quality, which, in turn, can negatively impact men's reproductive health. Numerous studies indicate that psychological stress worsens semen parameters and hormonal imbalances, such as reduced testosterone levels, further impairing semen quality. Consequently, these changes increase the risk of IVF failure, where semen

quality is critical for fertilization and embryo development. Therefore, stress reduction and improved sleep quality are essential elements in enhancing the success of assisted reproductive procedures [4, 23]. In conclusion, sleep disorders negatively impact couples' fertility through both biological and psychological mechanisms. Improving both partners' sleep quality and implementing stress reduction strategies are crucial for enhancing reproductive potential. Awareness of sleep's role in reproductive health should be an integral part of care for couples struggling with infertility [3, 4].

THE RELATIONSHIP BETWEEN SHIFT WORK, SLEEP DISORDERS, AND REPRODUCTIVE HEALTH

Shift work, especially during nighttime hours, disrupts circadian rhythms, affecting various biological functions, including reproductive health. The circadian rhythm regulates the secretion of key sex hormones such as testosterone, estrogens, and progesterone. Sleep disturbances caused by shift work can contribute to fertility issues in both women and men [2, 24, 25]. Shift work leads to sleep deprivation, circadian desynchronization, and suppression of melatonin secretion. These factors contribute to glucose intolerance and insulin resistance, which may result in miscarriage. Additionally, increased oxidative stress raises FSH levels, leading to anovulation and amenorrhea. Circadian rhythm disruption also promotes hyperprolactinemia, which causes anovulatory cycles and menstrual disorders. Shift work affects the secretion of sex hormones, lowering progesterone and LH levels while increasing estradiol, potentially resulting in infertility [2]. A study by WonYang Kang and colleagues examined the relationship between insomnia and menstrual irregularities in newly employed shift-working nurses. Over one year, 287 nurses were monitored. Statistical analysis revealed that those suffering from insomnia had more than twice the risk of experiencing menstrual irregularities compared to those without sleep disturbances [9]. Preeclampsia, miscarriages, preterm births, and other pregnancy complications can also be linked to shift work. Pregnant women working daytime shifts are twice as likely to avoid miscarriages compared to those working night shifts. According to one study, women working in shift patterns experienced six more miscarriages per 100 pregnancies compared to daytime-only workers [26]. The relationship between shift work and preterm birth is complex. Some studies suggest that extended working hours, variable schedules, standing positions, and intense physical effort may have a limited impact on the risk of preterm birth or small-for-gestational-age (SGA) infants. However, scientific evidence on this matter remains inconclusive [27]. In conclusion, pregnant women employed in shift work should consult their healthcare providers to assess individual risks and

adapt their work schedules to meet their needs during pregnancy.

An article by M. K. Demirkol evaluated the effects of shift work on semen parameters and sleep quality in men seeking infertility treatment. A study involving 220 men found that shift workers more frequently exhibited oligozoospermia and teratozoospermia compared to those with fixed work schedules. Additionally, a positive correlation was observed between sleep duration and sperm count, while a negative correlation was found between sleep latency and total sperm count. It was also demonstrated that night-shift workers had elevated serotonin levels in their blood due to disrupted circadian rhythms, which negatively affected semen parameters [28]. However, testosterone levels remained unchanged, suggesting no direct link between sleep quality and serum testosterone levels in shift workers [28, 29]. Conversely, a study by Kohn and colleagues, which focused on infertile men, observed that shift workers had lower testosterone levels, reduced sperm concentration, and fewer total motile sperm compared to infertile men with fixed work schedules [30]. It is worth noting that shift work can negatively impact sexual life by reducing the time, opportunity, and desire for sexual activity, further decreasing the likelihood of conception [28, 31, 32].

In conclusion shift work, especially during nighttime hours, adversely affects reproductive health in both women and men, primarily by disrupting circadian rhythms and reducing sleep quality. Awareness of these risks and implementing appropriate strategies can help mitigate the negative impact of night work on fertility.

POSSIBLE INTERVENTIONS AND RECOMMENDATIONS

THE IMPORTANCE OF SLEEP HYGIENE FOR IMPROVING REPRODUCTIVE HEALTH

Sleep hygiene, a set of habits and strategies aimed at improving sleep quality, plays a key role in maintaining reproductive health. Sleep influences many biological processes, such as hormonal regulation, cellular regeneration, and stress control. Adopting proper sleep-related habits can significantly enhance reproductive functions in both women and men, as well as improve the effectiveness of assisted reproductive techniques. Recommendations for sleep hygiene include reducing the consumption of caffeine, alcohol, and heavy meals in the evening. Maintaining consistent sleep schedules is crucial for supporting circadian rhythm synchronization. Avoiding blue light exposure by refraining from using electronic devices 1–2 hours before bedtime is also essential. Creating optimal bedroom conditions, such as darkness, silence, and a comfortable temperature, facilitates falling asleep and ensures

uninterrupted sleep. Regular physical activity during the day further aids in regulating the circadian rhythm and improving sleep quality [33].

POTENTIAL THERAPIES AND INTERVENTIONS

Melatonin, a hormone responsible for regulating circadian rhythms and protecting reproductive cells from oxidative stress, is commonly used for individuals with disrupted sleep rhythms (e.g., due to shift work) and patients undergoing assisted reproductive procedures such as in vitro fertilization (IVF). Studies suggest that melatonin supplementation can improve the quality of oocytes and sperm, as well as increase the likelihood of successful embryo implantation [2, 4, 34, 35].

Another promising method for managing insomnia is cognitive-behavioral therapy for insomnia (CBT-I). This evidence-based therapy combines behavioral interventions aimed at regulating sleep patterns with cognitive techniques focused on changing maladaptive beliefs and thoughts about sleep. CBT-I helps reduce reliance on sleep medications and mitigates the risks associated with their use. According to the American College of Physicians (ACP) guidelines, CBT-I should be recommended as the first-line treatment for all patients with chronic insomnia [36].

The Mindfulness-Based Program for Infertility (MBPI) is a psychological intervention designed for women struggling with infertility. Research indicates that MBPI effectively reduces psychological stress related to infertility. Participants report improved emotional well-being, reduced anxiety levels, and enhanced quality of life. Additionally, the program fosters psychological resilience, making it easier to cope with the challenges of infertility treatment [37].

Some cases of insomnia require pharmacological treatment. Various classes of medications are used, including benzodiazepines, non-benzodiazepine sedatives (so-called Z-drugs), melatonin and its receptor agonists, sedating antidepressants, and antipsychotics with sedative properties. Pharmacological treatment should be limited to 2–4 weeks and conducted under strict medical supervision to minimize the risk of side effects and dependency [38]. In summary, promoting sleep hygiene and employing appropriate therapeutic interventions, such as melatonin supplementation, CBT-I, or relaxation techniques, play a crucial role in supporting reproductive health. These measures can not only enhance natural reproductive processes but also improve the effectiveness of infertility treatments. Educating patients about the importance of sleep for reproductive health should be an integral part of care for individuals facing fertility challenges [2, 4, 34, 35, 36, 37, 38].

CONCLUSIONS

Sleep disorders significantly impact reproductive health, affecting both physical and mental well-being. In both women and men, sleep disturbances lead to hormonal imbalances, reduced reproductive cell quality, and decreased reproductive capabilities. Coexisting factors such as obesity, stress, and shift work further exacerbate these negative effects, increasing the risk of infertility.

Research indicates that improving sleep quality through sleep hygiene practices, melatonin supplementation, CBT-I, and mindfulness techniques can significantly support reproductive abilities and enhance the success of infertility treatments, including assisted reproduction methods. Stress reduction, often a key factor in sleep disturbances, is crucial for improving reproductive potential.

Education on the importance of sleep and its influence on fertility should become an integral part of care for individuals dealing with reproductive issues. Implementing strategies to improve sleep quality and reduce stress can support natural reproductive processes and increase the success of infertility treatments, such as IVF. Further research into the relationship between sleep and fertility is essential to better understand these connections and develop personalized therapeutic approaches.

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