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Depression and Stress Induced Infertility: A Review in Unisex

Gnanaraj VDP[1], Manohar SS[2], Dharmaseelan SE[3], Kandhasamy K[4]

[1,2,3]Doctor of Pharmacy, JKK Nattraja College of Pharmacy, Namakkal, Tamilnadu, India; [4]Associate Professor, Department of Pharmacy Practice, JKK Nattraja College of Pharmacy, Namakkal, Tamilnadu, India.

ABSTRACT

Today, infertility has become more common among young adults due to various reasons which are not easy to determine. The prevalence varies significantly in different parts of the world, ranging sparingly from less than 5% to over 30%. The recent trending cause estimated is the depression and stress due to occupational work. Infertility caused by depression and stress may further cause depression which again worsens the condition. This being the social problem, mass attention has to be achieved in terms of research for resolving it. Many researchers explained the neurophysiology of stress-induced infertility and its probable treatment whereas the exact reason and solution is still a question. In this review, we focus on the neurophysiology, infertility experienced by different occupational workers and the management of stress-induced infertility. A structured and orderly means were undertaken as a key aspect for the systematic literature review.

Key Words: Infertility, Stress, depression, Anxiety, Occupation, Hormones

INTRODUCTION

Infertility is a common term that resonates in every part and parcel of the world. To define infertility in the terms of the World Health Organization (WHO), it, specifically, is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.[1] In the year 2002, the WHO estimated that infertility affects approximately 80 million people all over the world.[2] Bovin et al., in 2007, suggested that nearly 72.4 million couples experience fertility problems.[3] This crucial problem is estimated to affect 10-15% of couples in the course of their lifetime.[4,5] The prevalence varies significantly in different parts of the world, ranging sparingly from less than 5% to over 30%.[3] The major breathtaking estimation is announced by the WHO, that approximately one in every ten couples has primary or secondary infertility. It is essential to identify the clear relationship between age and infertility. The Centre for Disease Control and Prevention (CDCP) reports that in the United States, infertility affects married women, independently from race and ethnicity, approximately with these percentages: 11% of women aged 15-29 years, 17% of women aged 30-34, 23% of women aged 35-39 and 27% of women ages 40-44.[6] Moreover, few authors have deliberately come forward to report that the probability of conception decline with age.[4,5,6]Apart from all these studies, the causal role of psychological disturbances in the development of infertility is still a matter of debate for ages. Anxiety in infertile couples was considerably higher than the general public, with 8%–28% of infertile couples showing substantial clinical anxiety.[7]

DISCUSSION

Neurophysiology of stress-induced infertility

Intriguingly, neurotransmitters and nuclei within the hypothalamus control stress and reproduction. Gonadotropin-releasing hormone (GnRH) neuron recruitment and activity is regulated by a balance between stimulation, suppression and permissiveness controlled by noradrenaline (NA), neuropeptide Y (NP-Y) and serotonin (5-HT) from the brain stem, impact from glutamate in the medial preoptic area and NP-Y in the arcuate nucleus (AN), in opposition to the restraining influences of Gamma-amino benzoic acid (GABA) within the medial preoptic area and opioids from the AN. Also, Stress activates NP-Yperikarya in the AN and brain stem NA

Corresponding Author:
Dr. K. Krishnaveni, Associate Professor, Department of Pharmacy Practice, JKK Nattraja College of Pharmacy, Namakkal, Tamilnadu, India.
Phone: 9965179049; Email: venidhiya@gmail.com

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neurons. The latter project indirectly, via the medial preoptic area, or directly to the paraventricular nucleus (PVN) to release corticotrophin-releasing hormone (CRH) and arginine vasopressin (AVP). Stimulation of CRH neurons in the PVN also activates GABA and opioid neurons in the medial preoptic area and reduces GnRH cell recruitment, thereby decreasing GnRH pulse frequency. Oestradiol enhances stress-induced NA suppression of luteinizing hormone(LH) pulse frequency but when applied in the PVN nucleus or brain stem, and not in the medial preoptic area or AN. Another stress-activated pathway involves the amygdala and bed of the nucleus stria terminals, which contain CRH neurons and accumulate GABA during stress.[8] Although both adrenocorticotropic hormone(ACTH) and glucocorticoids (GCs) are elevated in stress, there is little evidence that these hormones directly affect gonadotropin (Gn) secretion or ovulation.[9]

In normal intact animals, estradiol activation of GnRH–LH surge secretion involves an initial stimulatory oestradiol signal but restraining modulation is mediated by NA and opioid regulation of suppressive GABA neurons. During the later transmission phase in which oestradiol concentrations are higher, gradual removal of opioid influence may mediate the uncoupling of NA restraint on GABA cells, resulting in a (now oestradiol-independent) more positive NA influence on GnRH–LH release. At the end of the transmission phase, neurotransmitters control the recruitment of more GnRH neurons, culminating in coordinated hyperpolarization and massive outpouring of GnRH into the portal capillaries to cause secretion of the prepared stores of LH. Several reproductive situations involve suppression of GnRH–LH pulsatility mediated by increased sensitivity to oestradiol in different parts of the hypothalamus and brain stem. [8]

Effect of occupational stress on infertility

Industrial chemist

In today's economically fast-moving world, with an increasing number of women entering the workforce worldwide, women are exposed to various reproductive toxins. An increasing body of evidence shows a correlation between environmental and occupational exposures and reproductive adverse effects. Eventually, studies have examined the adverse effects of exposures to cigarette smoke,[10,11]caffeine[12] pesticides,[13,14] air pollution,[15,16] organic solvents,[17-22] and occupational stress.[23] The National Institute for Occupational Safety and Health estimated that 9.8 million workers in the United States were occupationally exposed to solvents. Organic solvents identified as potential reproductive toxins include benzene,[17,18,24] toluene,[19,20,21] and related compounds.[22] Studies have begun to suggest that even low-level occupational exposure to organic solvents is linked to a broad range of adverse reproductive outcomes which is shocking.[24,25] There is growing evidence that many environmental and occupational factors are associated with reduced birth weight.[26,27] As it is evident, benzene is known to produce several toxic metabolites that affect rapidly growing cells such as bone marrow, cause oxidative damage in the cells, and suppress cell growth.[28,29] Likewise, benzene and other organic aromatic solvents were repeatedly shown to be fetotoxic in animal studies, leading to delayed fetal growth and decreased birth weight.[30,31] The mechanism by which maternal stress affects birth outcomes was thought to be through stress-dependent hormones or immunological pathways.[32]

One notion that is least bothered is that the critical period before conception and during pregnancy is an important period for adverse influence on fertility and pregnancy outcome and that environmental tobacco smoke, and exposures from video display terminals (VDT) and indoor air quality, are the most common concerns of women in their places of work. Benzo[a]pyrene from pulmonary arterial hypertension (PAH) in tobacco smoke and diesel exhaust cause meiotic maturation of oocytes and deoxyribonucleic acid (DNA) adducts in sperm, oocytes and embryos of IVF patients. Polychlorinated biphenyl (PCB)from oils, electric coolant causes the impaired response to ovulation induction, reduced parity, impaired lactation, and potentially reduced fecundability. Further, dioxins and polychlorinated dibenzofurans (PCDF) from the incineration of plastics, automobile exhaust, and pesticide manufacturing cause potential for change in sex ratio and increased risk of endometriosis. Pesticides, usually from herbicides used in combination, cause no apparent effects alone but decrease in semen content and fecundity, spontaneous abortion, preterm birth, and low mixtures for gestational age. Also, Dichlorophenyl(tri/di)chloroethylene (DDT/DDE) cause reduced parity, impaired lactation, decreased semen quality, impaired fertility, and small-for-gestational-age babies. Decreased sperm counts & infertility are caused by Dibromochloropropane. Even lead and various metals cause decreased semen quality, increased time to pregnancy, and spontaneous abortion.[33]

Another important factor is physical load and heavy physical work (high energy expenditure) which cause spontaneous abortion, low birth weight. And frequent heavy lifting cause pre-term birth, spontaneous abortion. Prolonged standing results in low birth weight, pre-term birth, spontaneous abortion. Physical factors like ionizing radiation induce spontaneous abortion, congenital defects and reduced sperm count azoospermia. Similarly, noise (0.90 dBA)can also cause spontaneous abortion, low birth weight, pre-term birth.[34]

Oncopharmacist

While infertility was reported as an effect of chemotherapy for some cancer patients, there was no investigation into the connection of infertility with occupational exposure. Self-reported infertility is consequently associated with occupational handling of chemotherapeutic drugs before onset of

infertility. Most importantly, prevention of chemotherapy side effects by the use of available protection is preferable to risking infertility.[35]

Flight attendant

In the case of flight attendants, cosmic radiation and circadian disruption are potential reproductive hazards.[36] Miscarriage was associated with flight attendants who work during sleep hours and people who work under high physical job demands and who are associated with work under cosmic radiation exposure.[37,38,39] and menstrual irregularities.[40] Workplace exposures of concern include cosmic ionizing radiation[41] and circadian rhythm disruption.[42] Galactic cosmic radiation generates secondary and tertiary radiation at aircraft altitudes,[43] including neutrons and energetic photons (International Agency for Research on Cancer (IARC)-known human [group 1] carcinogens). One should note that the solar particle events (transient solar surface eruptions) are also another source of cosmic radiation exposure. To put together, flying across time zones or working during normal sleep hours can affect reproductive hormones with circadian regulation.[44]

Nurses

Shifts in circadian rhythms may play a role in regulating the reproductive hormones which control the menstrual cycle, either through sleep disturbances or through altered melatonin development. Shift work is even more prevalent among nurses, 24–28% of whom work in the evenings, nights, or rotating shifts. Most studies examining the relationship between shift work and menstrual cycle characteristics support an association between working at night and menstrual function. So night work, long hours, and physically demanding work might relate to menstrual disturbances. The sober thing is that the menstrual cycle is a marker of general reproductive health.[45]

Inhalation anaesthetist

Inhalation anaesthetics are commonly administered to veterinary patients. Some of these agents can enter the operating room atmosphere, exposing veterinary personnel to potential risks from chronic exposure to inhalation anaesthetic gas concentrations. Epidemiological studies of humans and laboratory studies of animals have suggested that chronic exposure to trace levels of anaesthetics may constitute health hazards including fetal death, spontaneous abortion, birth defects and cancer. A significant difference is noted in reproductive risk for women working in veterinary anaesthesia when compared to women working in veterinary critical care.[46]

Military personnel

A person in the military is often subjected to work-related stress or life event stress which result in alterations in their menstrual function. The study suggests that women in the military report less day-to-day job stress but more atypical life events, including those related to their jobs, and that these life events, in the long run, are associated with adverse menstrual consequences.[47]

Psychological distress in the workplace

Psychological distress has long been suspected of having an important impact on infertility.[48-53] In both sexes, psychological factors were found to be predictors of the couple's fertility status.[50-53] However, it is not yet well known if psychological stress is part of the aetiology of infertility as a causal factor or occurs as a consequence of the overall question of infertility. While other aspects of work, primarily exposure to chemicals, radiation, etc., have been studied, the effect of working conditions and psychological distress in the workplace on female infertility is a significant but less researched aspect of infertility. Occupational stress likely serves as an etiological factor among the male population, although it may be a piece of advice in women. The social responsibility for reproduction and treatment falls even more on women's shoulders than on men. On the other hand, it is possible that choosing a career delays conception and thus recognition of their infertility occurs only at an older age.[54]

Effect of stress on semen quality

Reports affirm that mental stress causes an abnormality of spirogram parameters. Nitric oxide (NO) is a highly reactive free radical gas that has been demonstrated to have an exceptional range of biological functions.[50] NOS has been found in the male reproductive system.[56] Being both a cytotoxic and necessary molecule for normal sperm production, NO has a dual function. Under physiological conditions, NO plays an important role in normal sperm production and motility. Low NO concentrations have been shown to enhance sperm motility,[57]whereas high NO concentrations reduce it.[58]Extrahepaticarginase may play a role in reactions other than those of the urea cycle.[59] Since arginase is an arginine-depleting enzyme, it is an important part of the cellular arginine regulatory system affecting NOS activity.[60] Psychological stress causes an increase of NO level and a decrease of arginase activity in the L-arginine-NO pathway. In addition, the poor quality of the sperm may be due to excessive NO production under psychological stress. Thus the arginine-NO pathway, together with arginase and NO synthase, are involved in semen quality under stress conditions.

Stress-induced effects also tend to include meiotic and structural changes in the sperm cells. The spermatogenic process was enhanced after a period of Modulating Radiance Therapy (CRM therapy) conveyor suggesting stress is an important risk factor for idiopathic infertility.[61] Identifying the psychosocial risk factors such as stress for poor semen quality is

important for improving fecundity and fertility, and may also have implications for the life course and intergenerational health.[62] In studies examining life stress, one prospective study found no association,[63] and another study found positive results for only one particular stressful life event (death of a family member),[64] and others were inconsistent with the semen parameter which found an association.[64-67] Similarly, a detailed analysis of stress at work found an inverse correlation with semen quality,[68] yet two others have not.[63, 64]

Management

Oxidative stress is thought to have an impact on male fertility and on normal embryonic development in the male germline. Fertility specialists are therefore actively investigating the treatment of such stress in spermatozoa and evaluating the potential use of antioxidants to relieve this disorder. The antioxidant efficacy of vitamin-C alone on sperm oxidative stress was first demonstrated[69] in a small number of smokers. Vitamin E, on the other hand, was found to effectively reduce ROS concentration and improve fertilization or pregnancy rates. The positive effects of zinc on semen parameters have been known for some time and documented in at least five clinical studies.[70-74] research recently showed the antioxidant efficacy of zinc in reducing multiple oxidant stress measures and increasing motility in asthenospermic patients.[75] Thus, the quest to identify novel antioxidants and combinations that are optimized for safety and efficacy is likely to continue. On theoretical grounds, an appropriate combination of antioxidants should be more effective than any single antioxidant since oxidative stress is a non-localized heterogeneous phenomenon. For example, vitamin-C, carnitines, zinc and NAC are all highly hydrophilic molecules; conversely, vitamin-E and carotenoids such as astaxanthin are highly lipophilic structures. Each of these naturally occurring antioxidants with their unique pharmacodynamic profile for the male reproductive tract is likely to neutralize at least some of the nearby ROS, therefore it transpires collectively to more effective management of sperm oxidative stress.[76]

Owing to hormone disorders, auricular acupuncture appears to offer useful alternative treatments for female infertility. As Cindy Margolis puts it, “Infertility is a massive roller coaster of emotions.” Psychological intervention is not only necessary to alleviate negative psychological symptoms, to escape anxiety, depression and phobia, but also to improve physical health and healthy pregnancy. Psychosocial counseling should be offered frequently at any stage of infertility treatment, and not only when treatment fails.[77] High glucose levels in the blood lead to hormone disruption as there is weight gain and insulin resistance in the body. Hormonal imbalance cause ovary dysfunction which may further cause depression and hence glucose level has to be maintained. [78]

CONCLUSION

Infertility is a global problem everyone as an individual should show attention in resolving the problem. The risk factors explained above should be considered and lifestyle changes should be adopted concerning the occupation.

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Conflict of Interest

There are no conflicts of interest.

Authors’ Contribution

DPG Vimala has helped develop the concepts, acquire knowledge and analyse data. In the literary quest, SM Sharumathi contributed. Ebenezer D Sam helped prepare the manuscript. The manuscript was examined by K Krishnaveni and revised.

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