ISSN 2380-3940

WOMEN'S HEALTH
OpenJournal

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PUBLISHERS

Review

Integrative Medicine Approaches in Irritable Bowel Syndrome, Painful Bladder Syndrome and Infertility in Women Health

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Article information

Received: May 12th, 2022; **Revised:** May 26th, 2022; **Accepted:** June 1st, 2022; **Published:** June 2nd, 2022

Cite this article

Baptiste-Weiss T, Cuzin B, Schmidtberger K. Integrative medicine approaches in irritable bowel syndrome, painful bladder syndrome and infertility in women health. *Women Health Open J.* 2022; 8(1): 1-8. doi: 10.17140/WHOJ-8-146

ABSTRACT

Chronic pelvic pain syndrome (CPPS) is one of the common diseases in urology, gynecology, and gastroenterology. CPPS is a multifactorial disorder where pain may originate in any of the urogynecology, gastrointestinal, pelvic musculoskeletal, or nervous systems. The aim of this article is to sensitize general observation for all integrative medicine practitioner to analyze data for a best interdisciplinary approaches-oriented results for health orientation. Indeed, CPPS could be severe enough to limit functioning, unrelated to menstrual cycle, pregnancy, local trauma, or pelvic operations. This syndrome is one of the diseases shared by urology and gynecology. Its frequency is between 3% and 10%, and it is more frequent among women. The costs of treating CPPS were estimated at about $880 million annually. About 15% of women reported loss of workdays and 45% reported decreased work efficiency. This review aims at presenting an interdisciplinary overview on CPPS patients focusing on links between irritable bowel syndrome, painful bladder syndrome and infertility, to illustrate the relevance of integrative medicine. We propose an integrative approach to treating the diverse symptoms of irritable bowel syndrome (IBS) by combining the benefits of and need for pharmacotherapy with known complementary and alternative medicine (CAM) therapies to provide IBS patients with the best treatment outcome achievable.

Keywords

Complementary; Alternative; Integrative; Therapies; Interventions; Nutrition; Antioxidants; Herbs; Supplements; Biofeedback; Phytotherapy osteopathy; Acupuncture.

INTRODUCTION

Chronic pelvic pain syndrome (CPPS)[1] is a common disease in urology, gynecology, and gastroenterology. CPPS is a multifactorial disorder where pain may originate in any of the urogynecological, gastrointestinal, pelvic musculoskeletal, or nervous systems. This syndrome is unique in that it is a disease shared by both urology and gynecology.[2] Its frequency is between 3% and 10%, and it is more common among women.[3,4] The costs of treating CPPS are estimated at about $880 million annually.[5] About 15% of women reported loss of workdays and 45% reported decreased work efficiency.[6,7] This review was aimed at presenting an interdisciplinary overview on CPPS patients focusing on links between irritable bowel syndrome (IBS),[8] interstitial cystitis (IC) or painful bladder syndrome (PBS)[9] and infertility,[10,11] further illustrating the relevance to integrative medicine.[12] IC/PBS is common and may affect between 3 million and 8 million women and between 1 million and 4 million men in the United States.[13] IC/PBS ranges from 1 out of every 100,000 to 5.1 out of every 100,000 in the general population; however, updated epidemiologic research conducted in 2006 suggests that up to 12% of women may have early symptoms of IC. Infertility is a global health issue affecting millions of people of reproductive age worldwide. Available data suggests that around 186 million individuals have infertility globally, an estimated 15% of couples globally,[14] amounting to 48.5 million couples.

Indeed, CPPS can be severe enough to limit functionality, unrelated to the menstrual cycle, pregnancy, local trauma, or pelvic operations. Women's health needs evolve across their lives. It is important to work with healthcare providers who take this into

account when caring for women at different life stages. The aim of this article is to synthesize these general observations for integrative medicine practitioners and to further analyze the data for better interdisciplinary[15] and results[16] oriented health outcomes. We propose an integrative approach to treating the diverse symptoms of IBS, IC, and infertility by combining the benefits of and need for pharmacotherapy with known complementary and alternative medicine (CAM) therapies to provide IBS patients with the best treatment outcome achievable.

"*Integrative medicine and health reaffirm the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic and lifestyle approaches, healthcare professionals and disciplines to achieve optimal health and healing*".[17]

IRRITABLE BOWEL SYNDROME, CHRONIC PELVIC PAIN AND PAINFUL BLADDER SYNDROME

Irritable bowel syndrome and chronic pelvic pain (CPP) are both somatoform disorders with a high prevalence within the population in general. IBS is a gastrointestinal disease that negatively affects up to 20% of the population.[18] IBS is more commonly diagnosed in women than in men and in people younger than 50-years.[19,20] IBS has a clear gender difference,[21] as it affects more women than men, studies showing that women are three times more likely to have IBS compared to men.[22] Given the complexity of the therapeutic management of IBS, alternative non-pharmacological therapies are frequently offered to patients. IBS has led to increased use of conventional medical care, at an estimated cost of hundreds of billions of dollars/years.[23]

Both IBS and CPP also are similar concerning prevalence, the coexistence of mental and somatoform disorders, the common history of sexual and physical abuse in the past and their health are utilization. Sex-gender[24] differences demonstrate a diversity of physiological and psychological factors. The clinical presentation of symptoms as well as treatment strategies in women and men with IBS may differ.[25] IBS is more common in women than men because of the correlations between sex hormones, especially progesterone, and gastrointestinal function have been proposed as an explanation on why women are more affected[26] by IBS compared to men.[27] Despite limited comprehensive data, sex hormones are believed to contribute to these gender differences as well as cultural factors and gender[28] roles. Many studies have indicated that sex hormones affect the regulatory mechanisms of the gut-brain axis, stress response, visceral sensitivity and motility, intestinal barrier function, immune activation of intestinal mucosa, and gut microbiota. Women with IBS tend to report lower quality of life (QoL), more fatigue, depressed mood, less positive well-being and self-control, and higher-levels of anxiety than men with IBS. In general, most patients present a wide array of symptoms due to malabsorption that include diarrhea, abdominal pain, bloating, and weight loss. In women, this disease may impact menstrual and reproductive health. This complex clinical context and the low effectiveness of available medications prompt many patients to use complementary and alternative medicines, such as mind-body therapies (hypnotherapy, mindfulness/meditation, yoga, osteopathic medicine, chiropractic care, acupuncture, reflexology, etc.), dietary supplements, energy therapies, and body-directed therapies. Phytotherapy may have potential beneficial effects, as recently suggested for curcumin as anti-inflammatory action efficiency.[29]

Many of the symptoms of IBS in females are the same as those in males, but some women report that symptoms get worse during certain phases of the menstrual cycle. The symptoms include delayed menarche, constipation, diarrhea, bloating, urinary incontinence, pelvic organ prolapse, CPP, painful sex, worsening of menstrual symptoms, fatigue, stress, risk factors, diagnosis, takeaway, lumbago and intercostal pain, muscular contracture of the lower abdomen with spasm early menopause, secondary amenorrhea, infertility, recurrent miscarriages, and intrauterine growth restrictions.[30] In many cases the authors of this article also suggest investigations concerning ovarian cysts, which are regularly found in this type of associated pathologies.

Irritable bowel syndrome should be considered with large spectral observation, and screening tests should be performed on women presenting with menstrual and reproductive problems and treated accordingly. There is a connection between IBS and CPP. Many studies have examined the connection and there is a strong overlap between the two. The International Foundation for Functional Gastrointestinal Disorders (IFFGD) has found in studies that one-third of women with IBS reported having long-lasting CPP.

During consultation and medical investigations, we can observe menstrual irregularities, dyspareunia, abdominal bloating (often due to food allergies or intestinal problems such as coeliac disease),[31] spontaneous abortion, sexual problem sometimes associated with infertility, distorted pelvic anatomy, altered peritoneal function, altered hormonal and cell-mediated function, endocrine and ovulatory abnormalities lower backache, tenderness of breast, nausea and vomiting bloating. Non-gastrointestinal symptoms such as psychological comorbidity and autoimmune manifestations including psoriasis,[32,33] may also be the presenting symptoms.

Ovaries are female reproductive organs. One ovary is located on each side of the uterus in the abdomen. It is held in place by strong tissue or skin called a ligament (Utero-ovarian Ligament). When the ovary becomes partly or totally twisted around the ligament, named "*ovarian torsion or adnexal torsion*". The ovarian torsion is commonly seen in women of reproductive age but can occur in other age groups as well. The incidence of ovarian torsion ranges from 2 to 5% in patients who have surgical treatment for adnexal masses. The most common adnexal mass associated with ovarian torsion is an ovarian dermoid cyst.[34] This commonly happens during ovulation, and they often go away on their own. Many women could have had an ovarian cyst and be completely unaware. Although ovarian cysts can often go unnoticed, if symptoms do appear they can be quite similar to the symptoms of IBS.

Unexplained abdominal pain associated with female pelvic disorders can create a psychological trauma for the women. The mechanisms by which we perceive abdominal pain are varied

and complicated. Abdominal pain is generally classified as visceral pain, parietal (also known as somatic or somatoparietal) pain and referred pain. Visceral pain[35] is elicited by stretch (mechano) receptors in the smooth muscle of hollow organs. Referred pain occurs when visceral afferents share spinal cord segments with somatic afferents from a remote location. Referred pain is usually intense, and often lateralizing, sometimes complicating the differential diagnosis.[36]

Etiology is multifactorial, including environmental, genetic, and immunologic factors.[37] The environmental component is due to the presence of gluten proteins in the diet, including wheat, rye, barley, and oats. The incidence is high in Caucasians and low in Asians and African Americans. The incidence in first-degree relatives is 10%, suggesting a genetic etiology.[38]

Pelvic and abdominal female disorder can be caused by a combination of uro-gynecology failure associated with gastro disease, an immune-mediated disorder that may have few or no symptoms, which can however be well-investigated and successfully treated with integrative medicine approaches.

Chronic pelvic pain is associated with dysfunctions such as irritable bowel syndrome, IC/PBS, as well as other nonspecific chronic fatigue syndromes. CPP is also associated with mental health disorders, including posttraumatic stress disorder and major depressive disorder. The relationship between CPP and comorbid conditions is often the primary focus of its diagnosis and management.[39] Several studies have shown that there is significant hypersensitivity of mechanosensitive bladder afferents and alterations in the excitation and channel properties of bladder innervating dorsal root ganglia (DRG) neurons both during and following colitis. The precise mechanisms by which these changes occur are yet to be fully deduced; however, several mechanisms have been hypothesized, including direct sensitization of dichotomizing afferents, sensitization of DRG and spinal pathways, as well as indirect sensitization of peripheral afferents following the breakdown of the epithelial barrier and the induction of neurogenic inflammation.[40]

CLINICAL EVIDENCE OF ASSOCIATION

Chronic abdominal and pelvic pain are common debilitating clinical conditions experienced by millions of patients around the globe. The origin of such pain commonly arises from the intestine and bladder, which share common primary roles (the collection, storage, and expulsion of waste). These visceral organs are near one another and share common innervation from spinal afferent pathways. The symptoms of PBS often occur in episodes of increased intensity, known as "flares", followed by periods of remission. In severe cases, urinary frequency can occur more than 60 times a day during flares. Some foods and beverages, as well as tobacco, tend to make the symptoms worse. Women suffering from PBS may also suffer from additional pelvic pain due to spasms of the pelvic floor muscles, irritable bowel syndrome, fibromyalgia, migraines, asthma, environmental allergies, lupus, rheumatoid arthritis, endometriosis, vulvodynia, and anxiety disorders. There is no test for the diagnosis of PBS. Testing is done to rule out other possible causes of the symptoms of PBS such as bladder cancer, urinary stones, sexually transmitted diseases, or other gynecological problems.

Chronic abdominal pain, constipation, or diarrhea are primary symptoms for patients with IBS. CPPS and urinary urgency and frequency are primary symptoms experienced by patients with lower urinary tract disorders such as PBS. It is becoming clear that these symptoms and clinical entities do not occur in isolation, with considerable overlap in symptom profiles across patient cohorts. Moreover, patients are 100 times more likely to have concurrent IBS than healthy controls. Patients visiting a gynecological clinic with combined or individual symptoms of urinary frequency and/or urgency are significantly more likely to have concurrent IBS symptoms than age-matched healthy controls.

Infertility is defined as a disorder of the reproductive system described by lack of success in achieving pregnancy after more than a year of regular unprotected sexual intercourse. IBS has a clear gender difference, as it affects more women than men, studies showing that women are three times more likely to have IBS compared to men.[41] The correlations between sex hormones, especially progesterone, and gastrointestinal function have been proposed as an explanation on why women are affected by IBS to a larger extent compared to men.[42,43]

Moreover, the significant differences observed between patients with IBS and controls could not be explained by the fecundability or the frequency of the sexual intercourse as these two measured variables did not differ significantly in the two groups.

PATHOPHYSIOLOGY

Possible causes of infertility in IBS patients include obesity, IBS medication, smoking, alcohol consumption, poor nutritional habits, psychological factors.

Oxidative stress is a plausible mediator of the connection between both female and male fertility and IBS. However, the data lacks direct evidence to confirm this hypothesis. Nevertheless, it is recommended that certain levels of oxidative stress should not be exceeded to decrease IBS symptoms and increase the odds of conception given that generation of reactive oxygen species (ROS) is an aftermath of metabolically active cells.[44]

COMPLEMENTARY AND ALTERNATIVE MEDICINE

As we approach the twenty-first century, medicine finds itself in great trouble. An economic crisis of unprecedented proportions has engulfed health-care institutions, bringing changes that have alienated patients and eroded the job satisfaction of physicians. In a nutshell, conventional medicine has become too expensive. All over the world, insurance systems are breaking down.

As a discipline, preventive medicine has traditionally been described to encompass primary, secondary, and tertiary preven-

tion. The fields of preventive medicine and public health share the objectives of promoting general health, preventing disease, and applying epidemiologic techniques to these goals. Around 80% of the world's population is estimated to use traditional medicine, such as herbal medicines, acupuncture, yoga, indigenous therapies, and others.[45] CAM therapies are alternative types of healing outside the realm of conventional Western medicine.

Complementary and alternative medicine has steadily increased in popularity in the United States of America (U.S.A) new federal report reveals that Americans spend about $30 billion a year on complementary health approaches, from *ginkgo biloba* to yoga. An estimated 60 million Americans spend money on them each year, and 4.1 million children have used some type of complementary medicine, the report reveals. All in, the out-of-pocket costs for these types of therapies total $30.2 billion.[46] Americans spent $33.9 billion out-of-pocket on CAM according to a 2007 government survey.[47] CAM therapies account for approximately 1.5% of total health care expenditures ($2.2 trillion)[48] and 11.2% of total out-of-pocket expenditures (conventional out-of-pocket: $286.6 billion and CAM out-of-pocket: $33.9 billion on health care in the United States). CAM products, classes, and materials with the majority going to the purchase of nonvitamin, non-mineral, natural products such as fish oil, glucosamine and Echinacea account for $14.8 billion. U.S. adults also spent approximately $11.9 billion on an estimated 354.2 million visits to CAM practitioners such as acupuncturists, chiropractors, or massage therapists. To put these figures in context, the $14.8 billion spent on nonvitamin, nonmineral, natural products is equivalent to approximately one-third of the total out-of-pocket spending on prescription drugs, and the $11.9 billion spent on CAM practitioner visits is equivalent to approximately one-quarter of total out-of-pocket spending on physician visits.

Approximately 38% of adults use some form of CAM for health and wellness or to treat a variety of diseases and conditions, according to data from the 2007 National Health Interview Survey (NHIS).[49] The CAM component of the NHIS was developed by the National Institutes of Health's (NIH), National Center for Complementary and Alternative Medicine (NCCAM), and the National Center for Health Statistics (NCHS) part of the Centers for Disease Control and Prevention. The data provide estimates of the cost of CAM use, the frequency of visits made to CAM practitioners, and frequency of purchases of self-care CAM therapies. The global complementary and alternative medicine market size was valued at $82.27 billion in 2020 and is expected to expand at a compound annual growth rate (CAGR) of 22.03% from 2021 to 2028.[50]

Many patients and doctors are not satisfied with the efficacy of conventional treatment. CAM, widely accepted as adjuvant therapy for infertility in many Western countries, has met a medical need in the infertile population. However, its effectiveness and safety are still controversial. Complementary medicine is the most commonly used CAM for some diseases like infertility, largest chronic pain in last intention from the patient demands. Integrative consultations are useful for all women's health issues, ranging from hormone imbalances and chronic fatigue to mood disorders and chronic pain. To help stay healthy and promote wellness, healthcare specialists must work together to provide care that is safe and effective, proactive, and preventive. Feeling relaxation and tranquility, security, and optimism, and gaining awareness of tensions in their bodies and their bodies' signals that allowed women to feel 'whole'. These factors may help women actively monitor their posture and muscle tension thereby reducing and preventing pain.

Complementary and alternative medicines have been associated with a higher degree of symptom management and quality of life in IBS patients. Over the past decade, several important clinical trials have shown that specific therapies, hypnotherapy, cognitive behavior therapy, acupuncture, osteopathy, and yoga improved treatment outcomes in IBS patients.

A multidisciplinary approach for diagnosis and treatment seems to be most effective for symptomatic relief. The evidence for such interventions as psychological treatments including the use of complementary and alternative medicine techniques for CPP in women. A combination of treatments is usually required over time for the treatment of refractory CPP. The multifactorial nature of CPP needs to be discussed with the patient, and a good rapport as well as a partnership needs to be developed to plan a management program with regular follow-up. The promotion of a multidisciplinary approach which includes complementary and alternative medicine techniques in managing CPP in women seems to yield the best results.

Currently, CAM is gradually challenging the dominant position of traditional therapies in the treatment of infertility and many associated symptoms that represent the IBS. CAM claims that it can adjust and harmonize the state of the female body from an integrated approach to achieve a better therapeutic effect and has been increasingly used by infertile women. CPPS[a] in individuals is challenging for the patient as well as the physician, as the differential diagnosis can be complex. CPPS is of significant interest in urology and accounts for up to 2 million office visits per year in patients including women. Pain localization, which requires knowledge of gut development and innervation, is crucial to understanding the pathophysiology of abdominal pain. The location of the

Footnote

a. Keywords cross-searched with CPPS included: western medicine, complementary, alternative, integrative therapies, interventions, nutrition, antioxidants, herbs, supplements, biofeedback, phytotherapy, cranio-sacral and or structural osteopathy, chiropractic medicine, and acupuncture (Traditional Chinese Medicine), Ayurveda and Homeopathy Traditional Alternative, Medicine/Botanicals, Ayurveda, Apitherapy, Bach Flower Therapy, Naturopathic Medicine, Traditional Chinese Medicine, Traditional Korean Medicine, Traditional Japanese Medicine, Traditional Mongolian Medicine, Traditional Tibetan Medicine, Zang Fu Theory, Mind Healing, Autosuggestion, Hypnotherapy, Neuro-linguistic Programming, Self-hypnosis, Spiritual Mind Treatment, Transcendental Meditation, Body Healing, Acupressure, Acupuncture, Alexander Technique, Auriculotherapy, Autogenic Training, Chiropractic, Cupping Therapy, Kinesiology, Osteomyology, Osteopathy, Pilates, Qigong, Reflexology, Yoga, External Energy, Magnetic Therapy, Bio-magnetic Therapy, Magnetic Resonance Therapy, Radionics, Reiki, Therapeutic Touch, Chakra Healing, Sensory Healing, Aromatherapy, Music therapy, Sonopuncture, Sound Therapy.

pain, together with the clinical presentation, shapes the differential diagnosis and thus guides the evaluation and management. CPP, which remains relatively common, is associated with comorbidities such as irritable bowel syndrome, major depressive disorder, or pelvic inflammatory syndrome. This pelvic abdominal pain could be neglected or unexplained and could create psychological trauma for the women, mainly when associated to infertility. Various CAM therapies for CPPS exist including biofeedback, acupuncture, hyperthermia, and electrostimulation. Although many CAM therapies demonstrate positive preliminary observations as prospective treatments for CPPS, further exploratory studies including more randomized, controlled trials are necessary for significant validation as treatment options for this complex disorder.[50]

CONSEQUENCES OF PATIENT MANAGEMENT

IBS, PBS and infertility are three frequent conditions whose etiology is multifactorial, including environmental factors and diet. Each health care professional receiving these kinds of patients should promote a global approach: history, diagnosis treatment to improve management. Findings from clinical et preclinical studies illustrate links between conditions and could be helpful for management.

The pathophysiology of PBS is composed of multiple possible factors, including oxidative stress; therefore, reducing the oxidative stress by living a healthier lifestyle with a balanced diet, rich in micronutrients, limited in caffeine and alcohol, avoiding smoking, and maintaining a normal body mass index with regular physical exercise may promote fertility and help diminishing IBS symptomatology. Data suggests that citrus fruits, tomatoes, vitamin C, artificial sweeteners, coffee, tea, carbonated and alcoholic beverages, and spicy foods tend to exacerbate symptoms, while calcium glycerophosphate and sodium bicarbonate tend to improve symptoms.

Moreover, recent clinical and experimental evidence documenting the existence of "*cross-organ sensitization*" between the colon and bladder. In such circumstances, colonic inflammation may result in profound changes to the sensory pathways innervating the bladder, resulting in severe bladder dysfunction. It is tempting to imagine the exploitation of these neuronal pathways for the treatment of both conditions, and acupuncture has shown to be efficient for mitigating inflammation associated with PBS.[51,52] Furthermore, acupuncturists primarily view IBS as an imbalance within spleen and liver meridians. The spleen meridian is responsible for ensuring transformation and transportation of food, and therefore has a very strong connection with the digestive system but more specifically at the intestines level. When there is a spleen deficiency, the common signs and symptoms may include soft or loose stools, muzzy head, and tiredness.[53] This meridian is easily affected through excessive mental activity, irregular eating habits or damp foods such as wheat and dairy products. More recent studies have shown that both sham acupuncture and traditional acupuncture provide significant improvement of symptoms. This has been associated with increased levels of osteoprotegerin in both groups and tumor necrosis factor-like weak inducer of apoptosis (TWEAK) more so in sham acupuncture group. It is estimated that nearly 50% of IBS patients use complementary medicines,[54,55] with 59% who use acupuncture.[56]

Many patients present with these diseases in adulthood and experience a wide range of non-classical symptoms, some of which are specifically relevant to women's health, such as uro-genital women dysfunctions and unfavorable pregnancy outcomes. Body-directed therapies such as acupuncture and osteopathic medicine (particularly cranio-sacral therapy) may be beneficial for overall IBS symptoms and proof that clinical benefit of non-pharmacological interventions for IBS are appreciated from patients.[57]

CONCLUSION

Integrative medicine has emerged as a potential solution to the healthcare crisis. It provides care that is patient-centered, healing-oriented, and uses therapeutic approaches originating from conventional and alternative medicine. Further studies are needed to confirm the efficacy and safety of acupuncture, osteopathy, and other complementary medicine as an adjunct to assisted reproductive technology in this particular population. The place of integrative medicine approaches is essential for large efficiency for women with these associated pathologies that are clinically, anatomically, and physiology connected. Initially driven by consumer demand, the attention integrative medicine places on understanding whole persons and assisting with lifestyle change is now being recognized as a strategy to address the epidemic of chronic diseases bankrupting our economy. Skills include learning to develop appropriate healthcare teams that function well in a medical home, developing an understanding of the diverse healing traditions, and enhancing communication skills. An important challenge will be the definition of the optimal control groups to be used in non-pharmacological trials.

Symptom Observations

In a World Health Organization (WHO) study of 8500 infertile couples, female factor infertility was reported in 37% of infertile couples in developed countries, male factor infertility in 8%, and both male and female factor infertility in 35%.[58] The remaining couples had unexplained infertility or became pregnant during the study. The most common identifiable female factors, which accounted for 81% of female infertility, were:

Symptom Observations in Integrative Medicine

With advancing female age, there is an increase in the percentage of women with age-related infertility. In addition, other factors that may reduce fertility, such as leiomyomas, tubal disease, and endometriosis, also increase. A reduction in coital frequency with increasing age also impacts fertility (Box 1).[59]

CONTRIBUTORS

Mr. Thomas BAPTISTE-WEISS – Integrative Health Practitioner – Main investigator. Dr. Béatrice CUZIN – main Investigator.

Box 1

Reference "Symptom Observations"	Symptom Observations in Integrative Medicine
• Ailments from cares and worries • Ovulatory disorders (25%) • Endometriosis (15%) • Pelvic adhesions (12%) • Tubal blockage (11%) • Other tubal abnormalities (11%) • Hyperprolactinemia (7%)	• Irregular periods • Excess androgen • Polycystic ovaries • Excess insulin • Low-grade inflammation • Heredity • Infertility • Gestational diabetes or pregnancy-induced high blood pressure • Miscarriage or premature birth • Nonalcoholic steatohepatitis—a severe liver inflammation caused by fat accumulation in the liver • Metabolic syndrome—a cluster of conditions including high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels that significantly increase your risk of cardiovascular disease. • Type 2 diabetes (T2D) or prediabetes • Psychological comorbidity • Sleep apnea • Depression, anxiety and eating disorders • Abnormal uterine bleeding • Cancer of the uterine lining (endometrial cancer) • Pelvic pain • Amenorhea • Chronic lumbar pain • Food allergy • Gluten intolerance • Anger easily • Shrieking during anger • Amelioration from consolation • Sentimental • Vomiting sensation after eating • Weeping easily • Weeping when alone • Offended easily • Persistent thoughts • Fear of insects • Fear of misfortune • Tendency to catch cold • Desire for spicy food • Thirst increased • Lack of sexual vaginal sensations • Psoriasis • Bloating in the lower abdominal area • Nausea, vomiting or loss of appetite • Dizziness when standing up from a sitting position • Changes in the timing of menstruation • Very heavy vaginal bleeding • Change in bowel movements • More frequent urination • Weight gain • Pain during or after sex

Ms. Kandra SCHMIDTBERGER – Proofreader and editor of this article.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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