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Evidence-Based Management of Infertility in Women With Polycystic Ovary Syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a polygenic disorder with a variable phenotype that commonly affects women of reproductive age. It can significantly affect a woman's ability to conceive and her quality of life. Effective treatment includes a multidisciplinary team approach that addresses the physiological and psychosocial manifestations of the disorder. Nurses have an important role in promoting early detection, education, and identification of services and resources to improve a woman's fertility and lifelong health.

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Polycystic ovary syndrome (PCOS) is a common endocrine disorder and metabolic disturbance observed in 4% to 18% of women of reproductive age (March et al., 2010; Moran, Hutchinson, Norman, & Teede, 2011). Signs of the syndrome can present as early as puberty (Ehrmann, 2005; Franks, 2002). Women with PCOS experience absent or infrequent menses, infertility, acne, and excess hair growth, and ultrasound images show enlarged multicystic ovaries. Although the cause is uncertain, scholars have hypothesized that insulin resistance contributes to the development of PCOS and other chronic diseases such as cardiovascular disease, hypertension, metabolic syndrome, obesity, and type 2 diabetes mellitus (Dunaif, 1997; Steinberger & Daniels, 2003). Kahsar-Miller, Nixon, Boots, Go, and Azziz (2001) found that 24% to 32% of women with PCOS had a mother or sister with insulin resistance and symptoms of hyperandrogenism. However, the roles of inheritance, familial food preferences, and lifestyle patterns associated with the causes of this disorder remain unclear (Diamanti-Kandarakis & Piperi, 2005). The purpose of this article is to provide a brief overview of PCOS and the fertility challenges that women with PCOS encounter. In addition, measures that nurses can take to improve reproductive, maternal, and neonatal outcomes are discussed.

Pathophysiology of PCOS

A disordered ovarian environment characterizes PCOS. In women with PCOS, ovarian follicles arrest in a state of preovulation. This state of arrest is caused primarily by an overabundance of androgens, which impedes follicle growth and ovulation. Current opinion suggests that insulin resistance is the culprit because it is observed in many women with PCOS (Dunaif, Segal, Futterweit, & Dobrjansky, 1989; Johnson, 2014). Insulin resistance causes an abnormal response in the ovary that results in an increase in the amount of circulating androgens that lead to hyperandrogenism (Fritz & Speroff, 2011). Figure 1 shows the overall pathophysiology of PCOS.

Diagnostic Criteria for PCOS

Because PCOS is a syndrome of ovarian dysfunction with a wide range of symptoms, diagnosis of this disorder can be challenging. No single symptom or blood test can diagnose this

The goal of infertility treatment in women with polycystic ovary syndrome is to generate and ovulate one mature follicle.

multifaceted disorder. Therefore, clinical awareness is important to facilitate early diagnosis and management. For years, the medical and scientific communities debated the diagnostic criteria for PCOS. Finally, at the Rotterdam conference of 2003, co-sponsored by the European Society for Human Reproduction and the American Society for Reproductive Medicine, the diagnostic criteria for PCOS (commonly known as the Rotterdam Criteria) were defined. At a minimum, a woman with PCOS must present with two of three key clinical features: (a) hyperandrogenism (clinical or serum evidence of elevated circulating male hormones), (b) cystic ovaries on ultrasound imaging, and (c) chronic oligoovulation or anovulation (infrequent or absent ovulation; Rotterdam ESHRE/ASRM-Sponsored Polycystic Ovary Syndrome Consensus Workshop Group, 2004).

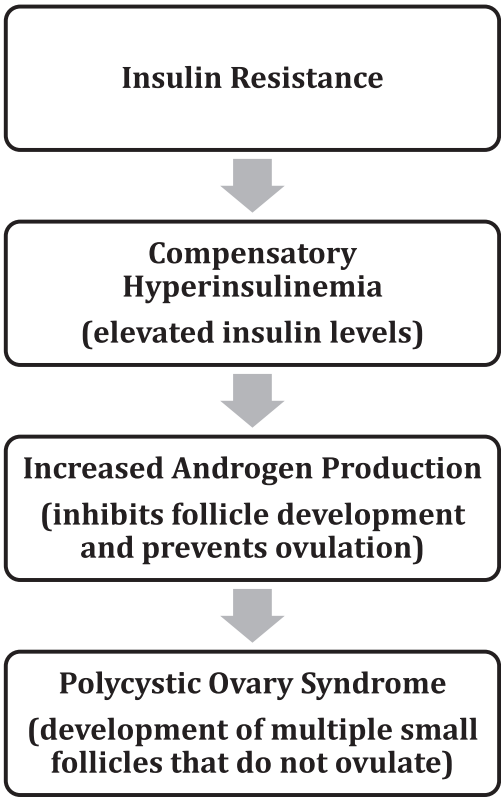

Figure 1. Pathophysiology of polycystic ovary syndrome.

Differential Diagnosis of PCOS

The clinical features of PCOS are similar to those of other disorders, and therefore diagnosis is made by exclusion. Nurses should be prepared to educate women about the diagnostic testing that will be ordered to exclude conditions that cause anovulation, such as hypothyroidism and hyperprolactinemia. If it is not clinically evident during the physical examination, tests for androgen levels such as testosterone assays are often required to confirm hyperandrogenism. In addition, referrals to clinicians specializing in reproductive endocrinology may trigger additional testing to rule out other etiologies such as Cushing's syndrome, hypothalamic amenorrhea, congenital adrenal hyperplasia, and androgen-secreting tumor. In general, the scope of testing reflects a woman's past medical and reproductive history and clinical findings.

Insulin Resistance

Insulin is a hormone that is essential for making glucose available for cellular metabolism. When muscle, fat, and liver cells become resistant to the action of insulin, the beta cells of the pancreas respond by pumping more and more insulin into the circulation to maintain glucose control. Higher levels of insulin can increase the production of androgens, such as dehydroepiandrosterone sulfate and testosterone, and interfere with the growth of ovary follicles. This compensatory hyperinsulinemia can be present for years without raising glucose levels. As androgen levels increase, ovarian dysfunction ensues, and hyperinsulinemia leads to weight gain and obesity. Obesity exacerbates the cardiometabolic consequences of PCOS and may result in fertility challenges. Excess weight contributes to increased time to conception, ovulatory dysfunction, lower implantation and pregnancy rates, higher miscarriage rates, and increased maternal and fetal complications (American Dietetic Association, 2009; Rich-Edwards et al., 1994; van der Steeg et al., 2004; Weiss et al., 2004).

Evidence demonstrates that increased insulin resistance may also be present in lean women with PCOS (Dunaif et al., 1989; Stepto et al., 2013). This syndrome correlates strongly with insulin resistance, which is a risk factor for type 2 diabetes mellitus in overweight and lean women. As such, recommendations include testing for glucose intolerance in women with newly diagnosed PCOS or those women not previously tested. In addition, many organizations, including

Table 1: Further Reading and Online Resources

American College of Obstetricians and Gynecologists. (2011). *Polycystic ovary syndrome*. Washington, DC: Author. Retrieved from http://www.acog.org/-/media/For%20Patients/faq121.pdf?dmc=1

American Society of Reproductive Medicine. (2014). *Polycystic ovary syndrome*. Birmingham, AL: Author. Retrieved from http://www.asrm.org/FACTSHEET_Polycystic_ovary_syndrome_PCOS/

Center for Young Women's Health. (2015). Home page. Retrieved from http://youngwomenshealth.org

Chavarro, J. E., Willett, W., & Skerrett, P. (2009). *The fertility diet: Groundbreaking research reveals natural ways to boost ovulation and improve your chances of getting pregnant*. Columbus, OH: McGraw-Hill Companies.

Futterweit, W., & Ryan, G. (2006). *A patient's guide to polycystic ovary syndrome: Understanding and reversing polycystic ovarian syndrome*. New York, NY: Holt, Henry & Company, Inc.

Grassi, A., & Mattei, S. (2009). *The polycystic ovary syndrome workbook: Your guide to complete physical and emotional health*. Haverford, PA: Luca Publishing.

Kimball, C., & Hammerly, M. (2003). *What to do when the doctor says it's polycystic ovary syndrome: Put an end to irregular cycles, infertility, weight gain, acne, and unsightly hair growth*. Gloucester, MA: Fair Winds Press.

the American Diabetes Association, the Endocrine Society, and the Androgen Excess Society, recommend that all women with PCOS be screened for type 2 diabetes mellitus and impaired glucose tolerance using a 75-g 2-hr oral glucose tolerance test (Legro et al., 2013). Type 2 diabetes mellitus, gestational diabetes, and impaired glucose tolerance occur more frequently in women with PCOS than in age-matched controls (Dunaif et al., 1989; Moran, Misso, Wild, & Norman, 2010).

Improvement of Fertility With Comprehensive Lifestyle Management

Lifestyle modification is widely accepted as the first line of treatment for women with PCOS to optimize their health before and concurrent with any fertility treatment (American College of Obstetricians and Gynecologists, 2009; Costello et al., 2012; Huber-Buchholz, Carey, & Norman, 1999; Moran et al., 2011). In fact, Mahoney (2014) studied women diagnosed with PCOS and fertility challenges and concluded that individualized comprehensive treatment plans guided by motivational interview techniques that are integrated into primary care and reproductive medicine visits are cost-effective approaches to intervene with lifestyle modification. Nurses are well positioned to develop and implement PCOS care plans that are best presented as multifaceted, lifelong, educational approaches to wellness. A good plan will address nutrition education, meal planning, physical activity, mental and emotional health, and weight and stress reduction strategies (Mahoney, 2014; Moran, Pasquali, Teede, Hoeger, & Norman, 2009). To facilitate engagement, nurses can provide patient-centered counseling with educational support in the form of electronic or written materials. Table 1 contains a list of resources.

In some studies, approximately 60% to 70% of women with PCOS in the United States were found to be obese (Azziz et al., 2004; Flegal, Carroll, Ogden, & Curtin, 2010; Glueck et al., 2005). Obesity is associated with PCOS and adversely affects reproduction. Evidence of adverse effects includes increased rates of anovulation, fertility treatment failure, pregnancy loss, and late-pregnancy complications in overweight women (Imani, Eijkemans, te Velde, Habbema, & Fauser, 1998; Overcash & Lacoursier, 2014; Pasquali, Pelusi, Genghini, Cacciari, & Gambineri, 2003). Helping overweight women with PCOS achieve weight loss is essential to their long-term health, especially when they are experiencing infertility, because the loss of as little as 5% to 10% of total body weight has been demonstrated to restore ovulatory and menstrual function (Clark et al., 1995; Homburg, 2003; Kiddy et al., 1992). Daily physical activity and dietary changes together with weight loss can help restore ovulation and enhance fertility for overweight and lean women with PCOS by increasing insulin sensitivity and thus lowering androgens (Legro et al., 2007; Moran et al., 2009). Nurses and clinicians should recognize that weight loss for most people is not easy, but for a woman with PCOS, weight loss is more difficult because of elevated androgens and insulin resistance. Androgens increase appetite and insulin, which is a growth hormone, and promote weight gain, especially in the abdomen (Barber, McCarthy, Wass, & Franks, 2006).

Table 2: Meal Plan Strategies for Increasing Fertility With Polycystic Ovary Syndrome (PCOS)

Recommendations	Metabolic Effect
Plan three meals plus two snacks per day. Avoid meal skipping. Eat breakfast. Distribute calories evenly throughout the day. Higher calorie breakfast and reduced intake at dinner are also beneficial (Jakubowicz, Barnea, Wainstein, & Froy, 2013).	Chronic meal skipping increases hunger, glucose levels, insulin resistance, weight gain, and metabolic stress. Distributing calories evenly maintains stable glucose levels, reduces cravings, and supports weight loss and weight maintenance. Larger breakfast and smaller dinner increases ovulation rate, improves insulin sensitivity, and lowers androgens.
Choose appropriate caloric intake for weight management in lean women with PCOS or weight loss for overweight women with PCOS (Grassi, 2007).	Lean women with PCOS should consume caloric intake that will maintain weight with daily activity. Overweight women with PCOS should reduce calories with modified carbohydrates, protein, and fat.
Follow individualized modified eating plan with guidance of registered dietician. Include low–glycemic-index and low–glycemic-load foods (Marsh, Steinbeck, Atkinson, Petocz, & Brand-Miller, 2010; Mehrabani et al., 2012).	With guidance from a registered dietician, modify carbohydrate, protein, and fat intake to lose weight at 1 to 2 lb per week with daily activity. Low-GI foods support lower fasting glucose, insulin, hemoglobin A1c, and triglyceride levels and increased satiety and insulin sensitivity.
Choose low-fat proteins at every meal and snack. Choose more plant-based protein. Include lentils and legumes; quinoa, bulgur, and whole grains; vegetables, nuts, seeds, and nut butters. Choose low-mercury fish and low-intake animal protein (Chavarro, Rich-Edwards, Rosner, & Willet, 2008; Grassi, 2007).	Combining low-fat protein with complex carbohydrates and heart-healthy fats supports lower glycemic meal response and greater satiety. Plant-based protein and low–saturated-fat protein intake supports fertility.
Choose complex, whole-grain carbohydrates for increased fiber to slow glucose absorption. Avoid or limit processed grains, juice, and snacks (Chavarro et al., 2009; Grassi, 2007; Marsh et al., 2010; Mehrabani et al., 2012).	Refined and processed carbohydrates are digested quickly and cause elevated glucose and insulin and, in turn, hyperandrogenism, which has a negative effect on ovulation.
Choose heart-healthy fats from nuts, seeds, olive oil, and low-mercury fish. Avoid hydrogenated (trans) fats. Limit saturated fats. Avoid palm and coconut oils (Chavarro et al., 2007, 2008; Grassi, 2007).	Hydrogenated (trans) fats contribute to cellular inflammation, oligomenorrhea, and insulin resistance. Trans and saturated fats increase low-density lipoproteins, cholesterol, and triglycerides. Elevated cholesterol decreases fertility. Heart-healthy fats promote hormonal balance.

At present, because of the many phenotypes of PCOS and its complex presentation, no consistent evidence is available to support a universally agreed-on meal plan for those diagnosed with PCOS (Moran et al., 2013). Because PCOS is the most common cause of ovulatory infertility, the research of Chavarro, Rich-Edwards, Rosner, and Willet (2007, 2008, 2009), who focused on the effect of diet on ovulatory dysfunction, may be useful. These researchers examined the dietary and fertility data of 18,555 nurses enrolled in the Nurses' Health Study and found that increasing insulin sensitivity through balanced low-glycemic food choices could improve ovulation. They also studied the effect of various meal plans on a woman's fertility and found that women who had the greatest intake of protein experienced 41% more ovulatory infertility, whereas those who had the greatest intake of highly processed grains increased their infertility by 50%. Women who consumed plant-based complex carbohydrates experienced the least infertility (Chavarro et al., 2008, 2009). Table 2 details additional meal planning strategies for hormonal imbalances and metabolic dysfunction.

The Role of the Nurse as Compassionate Educator

Women with PCOS should be screened for anxiety and depression, because these mood disorders may make the ability to cope with fertility challenges more difficult (Hahn et al., 2006; Weiner, Primeau, & Ehrmann, 2004). Psychological support and PCOS health and lifestyle education can empower women who may be overwhelmed by the enormity and permanence of a PCOS diagnosis. Nurses can use active listening skills to provide empathy, support, and encouragement to these women. Also, nurses can be sensitive to the fact that extreme disordered eating and exercise are prevalent in the PCOS population and are often used as ineffective means to deal with weight struggles and poor self-image. Nurses will find it helpful to have access to mental health referral information as a part of an effective interdisciplinary approach.

Nurses can encourage healthy eating and exercise behaviors through motivational interviewing without a focus on weight loss. Emmons and Rollnick (2001) defined motivational interviewing as a patient-centered counseling style that supports behavior change with reflective listening and objective feedback to elicit motivation from patients. Nurses and all members of the multidisciplinary team need to be aware that throughout their lifetimes, many overweight women have experienced weight bias, especially from practitioners in the medical community (Poon & Tarrant, 2009; Puhl & Heuer, 2009; Tomiyama et al., 2015). Weight loss and weight management are significantly more difficult for women with PCOS than women without PCOS. Taking time to listen and assess emotional and physical symptoms and offer praise for small changes will encourage women to be actively involved in their PCOS management plans. Body mass index (BMI) screening and weight loss interventions before pregnancy can be much easier to implement if a woman realizes that pregnancy may be more difficult to achieve without weight loss.

Regular Physical Activity Is Key

Physical activity is an essential modifiable lifestyle component in the management of PCOS. Consistent physical activity is effective to optimize fertility because movement lowers insulin, androgens, and lipid levels and, in turn, supports weight loss and ovulatory function. Several investigators examined additional exercise benefits in the reproductive presentation of PCOS. Palomba et al. (2008) demonstrated that dietary changes could influence greater weight loss and a decrease in adrenal androgens. However, compared with dietary changes, exercise alone caused a greater rise in sex hormone–binding globulin and a reduction in insulin resistance and testosterone and free androgen index levels. As part of a lifelong healthy lifestyle, exercise can improve overall metabolic parameters, mental health, self-image, and weight management in women with PCOS (Harrison, Lombard, Moran, & Teede, 2011).

Treatment plan expectations need to be realistic. For example, women should be encouraged to change their activity levels with gradual, simple steps to reduce physical injuries, exhaustion, and the frustration that can accompany slow weight loss. A consistent combination of a minimum of 30 minutes of activity five times per week and 20 minutes of weight resistant movement three times per week is enough to affect positive health changes before and during pregnancy (Banting, Gibson-Helm, Polman, Teede, & Steptoe, 2014; Lamb et al., 2011; U.S. Department of Health and Human Services, 2008). Nonpregnant or postpregnant women should understand the benefits of losing inches and maintaining even modest weight loss to achieve hormonal balance. In most cases, women with PCOS become more motivated to initiate and maintain physical activity when they understand the medical benefits of these measures as they relate to PCOS (Banting et al., 2014).

Medical Treatments for Infertility

Medications

Because oligoovulation or anovulation is the primary reason for infertility, the goal of treatment in women with PCOS who attempt pregnancy is to generate and ovulate one mature follicle. For lean women with PCOS or those women for whom lifestyle interventions are ineffective to restore ovulation, oral medications to treat anovulation are considered the second-line treatment (Homburg, 2003). The two most commonly prescribed oral ovulation induction agents are clomiphene citrate and metformin. However, some debate exists about which medication is more effective on reproductive outcomes. In a systematic review, Tang, Lord, Norman, Yasmin, and Balen (2012) found that the efficacy of metformin, particularly in obese (BMI $>$ 30 kg/m^2) women with PCOS, was consistent with an earlier

When working with women with polycystic ovary syndrome, nurses are in an ideal position to suggest lifestyle changes that will have significant, positive effects.

published review. Although metformin was associated with improved ovulation and clinical pregnancy rates, it did not improve live birth rates whether prescribed alone or in combination with clomiphene citrate (Tang et al., 2010, 2012). Currently, the U.S. Food and Drug Administration (FDA) has not approved metformin for the treatment of PCOS. Theoretically, however, metformin improves insulin sensitivity, which can decrease androgen levels and restore ovulatory and menstrual function (Romualdi et al., 2010). Usually when prescribed, metformin is titrated gradually to minimize the gastrointestinal adverse effects that are associated with higher dosages.

Clomiphene citrate is the oral ovulation induction agent of choice (Misso et al., 2012; Thessaloniki ESHRE/ASRM-Sponsored Polycystic Ovary Syndrome Consensus Workshop Group, 2008). It blocks estrogen receptors at the level of the hypothalamus, which alters gonadotropin-releasing hormone secretion and leads to an increase in follicle-stimulating hormone and ovulation. It is the only FDA-approved oral ovulation induction agent, and it has high ovulatory rates when administered at the proper dosage (Homburg, 2005). Clomiphene citrate is administered during the early follicular phase of the menstrual cycle or during a progesterone-induced withdrawal bleed. It is important to assess for evidence of ovulation to ensure that a woman has an opportunity for pregnancy. A luteal progesterone level greater than 3 ng/ml is consistent with ovulation.

For women who do not ovulate on the starting dosage of clomiphene citrate, the clinician may increase the daily dose. A change in therapy is recommended if a pregnancy does not occur after six ovulatory cycles on the drug (Thessaloniki ESHRE/ASRM-Sponsored Polycystic Ovary Syndrome Consensus Workshop Group, 2008). Because of its antiestrogenic properties, clomiphene citrate can be detrimental to cervical mucus and endometrial thickness, which may negatively affect conception and implantation. Nurses need to educate women about adverse effects that include hot flashes, dry mouth, and vision changes, which may require a change in medication management.

Approximately 20% to 30% of women do not ovulate while taking clomiphene citrate. For this group, the addition of metformin may be beneficial (Tang & Balen, 2013). Although the evidence is conflicting, some researchers have found that use of metformin is associated with reduced risk of a first-trimester spontaneous abortion (Nawaz, Khalid, Naru, & Rizvi, 2008). Other researchers found no clear data to suggest that metformin reduces pregnancy loss or improves pregnancy outcomes except in women with diabetes or diabetes mellitus type 2 (Mathur, Alexander, Yano, Trivax, & Azziz, 2008). As such, metformin is frequently prescribed during pregnancy in the subset of women with PCOS who have moderate to severe insulin resistance or do not respond to lifestyle and nutritional interventions (Mathur et al., 2008). The third ESHRE/ASRM-Sponsored PCOS Consensus Workshop did not recommend the routine use of metformin in PCOS patients (Fauser et al., 2012). The FDA categorizes metformin as a pregnancy category B drug, which confirms its efficacy and safety in immediate pregnancy outcomes. However, the long-term consequences are unknown. Currently, no published guidelines are available regarding the duration of metformin treatment in pregnancy, and management is based on individual clinical presentation (Lautatzis, Goulis, & Vrontakis, 2013).

Another promising option for this subset of women is a trial course of aromatase inhibitors. Aromatase inhibitors block the conversion of androgens to estrogens in the ovary. This decrease in estrogen levels provides negative feedback in the hypothalamus, which stimulates the pituitary gland to secrete follicle-stimulating hormone. The FDA has not approved aromatase inhibitors for ovulation induction. However, clinicians in reproductive endocrinology settings have been prescribing aromatase inhibitors off-label for more than a decade, and studies are encouraging regarding their effectiveness (He & Jiang, 2011; Mitwally & Casper, 2001). In a recent, double-blind, randomized, prospective, multicenter trial of 750 women ages 18 to 40 years diagnosed with PCOS, letrozole was more effective than clomiphene citrate. Legro et al. (2014) observed that 27.5% of women treated with 2.5 mg of letrozole for 5 days had term births, compared with 19.1% of women treated with 50 mg of clomiphene citrate daily ($p = .007$). Aromatase inhibitors have a shorter half-life than clomiphene citrate and are excreted from the body before any potentially damaging antiestrogenic effects can

occur on the cervix and uterine lining. These half-life and therapeutic effects make aromatase inhibitors a first-choice medication for many reproductive endocrinologists (Casper & Mitwally, 2011).

Laparoscopic Ovarian Drilling

Second-line therapies for clomiphene citrate–resistant women with PCOS include laparoscopic ovarian drilling and the administration of injectable gonadotropins (Costello & Ledger, 2012; Thessaloniki ESHRE/ASRM-Sponsored Polycystic Ovary Syndrome Consensus Workshop Group, 2008). Laparoscopic ovarian drilling is not common because it is a surgical procedure with all the accompanying medical and financial concerns. Laparoscopic ovarian drilling involves the use of a laser or electrocautery to drill four to 10 holes in the stroma of the ovary to cauterize the testosterone-producing tissue of the ovary. Gjonnaes (1984) first reported that a single treatment could restore ovulatory menstrual cycles in 92% of women and result in a 58% pregnancy rate. Since then, in a review of nine trials with 1,210 women, authors found no significant advantage in reproductive outcomes for women who underwent laparoscopic ovarian drilling compared with clomiphene citrate–resistant women who used other therapies, such as gonadotropins. However, compared with gonadotropin therapy, ovarian drilling eliminated the risk of multiple pregnancies and ovarian hyperstimulation (Farquhar, Brown, & Marjoribanks, 2012).

Injectable gonadotropin administration is more widely used because it is less invasive, does not require surgery or anesthesia, and is short-acting, thereby precluding any concerns about lasting effects on ovarian function. Injectable gonadotropins need to be used with caution in women with PCOS, because many mature follicles can develop and increase the risk for ovarian hyperstimulation syndrome and multiple gestations. Prevention strategies for ovarian hyperstimulation syndrome include frequent in-cycle monitoring with blood work and ultrasonography.

Assisted Reproductive Technologies

In many cases of PCOS, the safest and most effective means of achieving pregnancy is through assisted reproductive technologies such as in vitro fertilization (Chambers et al., 2010; Costello & Ledger, 2012; Reindollar et al., 2010). In general, most women with PCOS have multiple small follicles in the ovary, which often quickly respond to injectable gonadotropin medications. These highly responsive follicles swing between extremes of hyperstimulation and understimulation (Egbase, Sharhan, & Grudzinskas, 2002). Risks of hyperstimulation include the development of the potentially life-threatening condition of ovarian hyperstimulation syndrome and multiple gestations, including high-order (>2) multiple pregnancies.

In an in vitro fertilization cycle, stimulation medications produce multiple follicles with the expectation that many mature eggs will develop for subsequent retrieval and fertilization in the laboratory. Once mature, oocytes (eggs) are surgically retrieved from the ovary and fertilized in the embryology laboratory. The resulting zygotes, or early embryos, are incubated in an enhanced culture media. Mature blastocyst-stage embryos (day 5 or 6) are used for intrauterine transfer. However, if uterine dyssynchrony occurs, or if other reasons such as ovarian hyperstimulation prevent embryo transfer, the embryos can be frozen (cryopreserved) and transferred in a subsequent frozen embryo transfer cycle. Successful cryopreservation techniques have dramatically reduced the risk of hyperstimulation, and use of single-embryo transfer has reduced multiple gestations and births.

Dietary Supplementation Facts for Fertility

Over the past few years, dietary supplementation has gained in popularity. Evidence-based research exists related to a few popular supplements such as *myo*-inositol, *N*-acetylcysteine, vitamin D, and fish oil, which are administered for PCOS hormonal and metabolic symptoms (Costantino, Minozzi, Minozzi, & Guaraldi, 2009; Hahn et al., 2006; Macut, Bjekic-Macut, & Savic-Radojevic, 2013; Oner & Muderris, 2011, 2013; Papaleo, et al., 2007). Supplements are not a substitute for healthy dietary and activity recommendations or medications and are used only as adjunct therapy to optimize health and support fertility. Medications, health conditions, pregnancy, and surgery may contraindicate dietary supplements. Patients need counseling on how to use and choose safe supplements for their individual health and treatment plans (National Institutes of Health, 2014). Women should start quality prenatal vitamins 3 or more months before trying to conceive. Because patients often self-prescribe over-the-counter medications and supplements, nurses should inquire about the use of medications, vitamins, supplements, and

Pregnant women with polycystic ovary syndrome are at increased risk for maternal, fetal, and neonatal complications, which underscores the importance of preconception lifestyle and nutrition education.

herbal remedies at every visit. Table 3 provides a list of supplements.

Implications for Healthy Pregnancy in Women With PCOS

McBride, Emmons, and Lipkus (2003) labeled a health event that can influence individuals to make a positive change in behavior as a "teachable moment" (p. 156). Pregnancy is one example of a teachable moment, because women have an extra incentive to make healthy dietary and lifestyle changes to maximize the health of their infants. By the time an overweight or obese woman with PCOS presents for her first obstetric visit, the only option is to limit gestational weight gain, because weight loss during pregnancy is not recommended. Nurses who work with these women are in an ideal position to help them make the appropriate changes that can have significant positive effects on the outcomes of future pregnancies. However, despite efforts in the promotion of preconception changes, many women with PCOS enter their pregnancies with many of the same clinical, psychological, and behavioral issues. Moderate insulin resistance characterizes a normal healthy pregnancy even in women without PCOS. However, when insulin resistance is present before conception, as in women with PCOS, the effect is cumulative.

A pregnant woman with PCOS requires careful monitoring for the associated maternal and fetal morbidity related to insulin resistance. Complications include miscarriage, pregnancy-induced hypertension and pre-eclampsia, gestational diabetes, premature delivery, small size for gestational age, and increased rate of cesarean birth (Boomsma et al., 2006; Ghazeeri, Nassar, Younes, & Awwad, 2012). The obstetric risks alone require close observation of women with PCOS during pregnancy. In addition, as Barker (1995, 2004) and Drake and Walker (2004) hypothesized, the unfavorable uterine milieu associated with insulin resistance may influence fetal programming and translate into the development of chronic disease later in life for the infant. Thus, obesity and alterations in insulin and other hormones seen in women with PCOS may be markers for an increased risk of their offspring developing PCOS, diabetes, and atherosclerosis as adults (Boomsma et al., 2006; Drake & Walker, 2004; Legro, 2009). These observations emphasize how important it is for women with PCOS to strive for a healthy preconception BMI, limit gestational weight gain, and engage in regular exercise. Collaboration with a registered dietician or certified diabetes educator before and during pregnancy may also help reduce the risk of developing adverse obstetric and long-term medical outcomes.

Table 3: Supplements

Supplement	Description	Metabolic Effects
Myo-inositol	Member of the B complex vitamin group and a component of cell membranes	Improves insulin sensitivity, menstrual regularity, and ovulatory function and lowers androgen levels (Costantino, Minozzi, Minozzi, & Guaraldi, 2009; Papaleo, et al., 2007).
N-acetylcysteine	Antioxidant and an amino acid	Improves ovulatory function, hirsutism, fasting insulin level, and menstrual irregularity and lowers androgen, low-density lipoprotein and cholesterol levels (Oner & Muderris, 2011).
Vitamin D3	Fat-soluble vitamin and hormone	Vitamin D3 deficiency (<20 ng/ml) is associated with insulin resistance and a higher body mass index (Hahn et al., 2006).
Omega-3 fish oil	Essential fatty acid found in fish, also a vital component of human cell membranes	Improves hirsutism and insulin resistance. Lowers luteinizing hormone and testosterone. Increases sex-hormone binding globulin. Improves dyslipidemia. Reduces oxidative stress (Macut, Bjekic-Macut, & Savic-Radojevic, 2013; Oner & Muderris, 2013).

Conclusion

Polycystic ovary syndrome is one of the most common disorders that affect women of reproductive age. Paradoxically, it is also one of the most undertreated endocrine disorders in women. The primary goal of treatment is to manage insulin resistance, the underlying disorder that generates many of the negative sequelae associated with PCOS, including infertility (Grassi, 2007). Ways to manage insulin resistance include practicing stress management techniques, engaging in daily physical activity, adhering to medication and supplement recommendations, and following a healthy balanced meal plan. Polycystic ovary syndrome puts women at increased risk for maternal, fetal, and neonatal complications, underscoring the importance of striving for a healthy preconception BMI and minimizing gestational weight gain. Nurses who provide care to women of reproductive age desiring pregnancy should be familiar with the physical, social, and psychological challenges women with PCOS experience. These challenges are significant because they can affect a woman's ability to conceive and her lifelong health and quality of life.

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