

A Contraceptive Review and Update

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Abstract

There are many effective, well-tolerated, safe and readily reversible contraceptives. Clinicians should remain informed regarding contraceptive methods, including emergency contraception. The following is a concise summary of the important aspects of various contraceptives, including current recommendations for options that may be tailored to the unique needs of individual women.

Keywords: Long acting reversible contraceptives; Depot medroxyprogesterone acetate; Thrombogenic mutations; Dysmenorrhea

Introduction

Today's contraceptives are improved and highly effective, offering women more options to meet their reproductive goals. Clinicians should regularly assess individual contraceptive needs, compliance and provide education given the unintended pregnancy rate of 45% or 2.8 million (of the 6.1 million) U.S. pregnancies yearly [1]. Contraceptive choice is based on individual preference, ease of use, cultural or social factors, access and cost, menstrual and medical issues and planned timing of childbearing. The most effective methods include long acting reversible contraceptives (LARCS) as intrauterine devices (IUDs), subdermal implant and sterilization with less than 1% pregnancy rates followed by moderately effective methods as depot medroxyprogesterone acetate (DMPA) injections (less than 1% to 6% pregnancy rates with perfect and typical use), estrogen containing contraceptives (less than 1 to 9% pregnancy rates) and diaphragms (6 to 12% pregnancy rates) [2]. Contraceptive need continues through perimenopause with many methods additionally beneficial for heavy menstrual bleeding, dysmenorrhea and other gynecological concerns [3].

Oral pills, ring and patch

Most estrogen-containing contraceptives (ECCs) have ethinyl estradiol and various progestins with the newer progestational agents as drospirenone and cyproterone, having the least androgenic effects (helpful in Polycystic Ovarian Syndrome, PCOS) [2]. The ECCs work by suppressing ovulation, creating endometrial atrophy, thickening cervical mucus, inhibiting sperm permeability and impairing tubal motility [4]. After pregnancy is reasonably excluded, ECCs can be started on the day they are prescribed or the first day of menstrual bleeding. Back up contraception should be for 7-14 days with ECC initiation and when the progestin only pill is used, back up contraception should be for the first pill packet. The ECCs (including pills, patch and ring) can be used in a cyclic regimen with monthly menses versus extended-cycle regimen with menses occurring every 4th packet or after 12 weeks of continuous monophasic (generally fixed doses of ethinyl estradiol and progestin in hormonally active pills

versus multiphasic pills in which progestin varies in dosage across the hormonal pills) oral contraceptives (OCs). Formulations are available that contain 84 days of hormonal pills with 7 days of inert pills or formulations with no inert tablets. Break through bleeding, more common with extended-cycle regimens, often improves. For a missed pill, it should be taken when noticed and then the next pill taken when due. Back-up contraception is warranted if 2 or more consecutive pills are missed. In women with BMIs \geq 30 kg/m², there may be an increased risk of contraceptive failure, especially with the contraceptive patch, so daily compliance is important. Obese women are more likely to experience venous thromboembolism (VTE) with ECCs [2,4]. After discontinuing ECCs, menses should return within 90 days. If amenorrhea persists, it should be evaluated. Common estrogen effects as breast tenderness, nausea and bloating lessen with time and can be minimized with lower dose OCs (10-20 mcg) compared with slightly higher dose OCs (30-35 mcg).

Medical conditions contraindicated with ECCs are based on the U.S. Medical Eligibility Criteria for Contraceptive Use published by the Centers for Disease Control (CDC) (table available: Med Elig Crit, CDC) from World Health Organization (WHO) recommendations [2]. These include smoking after age 35, presence of arterial cardiovascular disease or known ischemic heart disease, complicated valvular heart disease, hypertension, history of cerebral vascular disease (CVA), VTE, known thrombogenic mutations, systemic lupus erythematosus, migraines with aura (any age), breast cancer, cirrhosis, and hepatocellular adenoma or malignant hepatoma.

Noncontraceptive benefits of ECCs include heavy menstrual bleeding, dysmenorrhea, chronic pelvic pain due to endometriosis, menstrual migraine without aura, PCOS, hypothalamic amenorrhea, premenstrual syndrome/premenstrual dysphoric disorder and perimenopausal vasomotor symptoms [3]. The estrogen containing OCs decrease the risk of endometrial and ovarian cancers, especially when used long term [4]. This protective effect may persist for 15 to 30 years after discontinuing OCs but is attenuated over time. In BRCA1 and 2 carriers, data are conflicting as to whether there is similar risk reduction.

Special Circumstances: Progestin-only OCs and other progestin methods do not impair lactation and can be used during breastfeeding. Progestin only OCs can be started immediately postpartum with ECCs recommended to be started no sooner than 30-42 days post-delivery

given VTE risk [2]. Studies show conflicting results with use of ECCs and lactation, and no consistent neonatal adverse effects. Estrogen containing OCs and some anticonvulsants are not ideal used together due to accelerated liver metabolism decreasing OC effectiveness (phenytoin, carbamazepine, topiramate, oxcarbazepine) or increased clearance of certain antiepileptics (lamotrigine) [2,4]. The LARCs or DMPA are better choices with anticonvulsants. Most antibiotics do not lessen the efficacy of ECCs except for rifampin and thus, no back-up contraception is required when using antibiotics and ECCs [2]. Contraception can generally be discontinued at age 52-55 given average menopause occurring at 51-52. A barrier method should be used temporarily in case of ongoing menstrual cycles.

Depot medroxy progesterone acetate (DMPA)

This injectable progestin-only contraceptive comes in 2 formulations: A 150 mg/1 ml intramuscular injection and as a 104 mg/0.65 ml subcutaneous injection (the latter can be self-administered) [5]. DMPA inhibits ovulation with similar cervical, endometrial and tubal effects as ECCs. Injections are given every 3 months (13 months) when pregnancy is reasonably excluded with a two-week "grace period" [2]. In women more than 2 weeks from last injection, pregnancy testing is recommended with back-up contraception for 7 days. Fertility returns in 50% of women by 10 months after last injection but some women may not reestablish fertility for 18 months. Unscheduled bleeding, the most common reason for discontinuation, often improves but if persistent requires evaluation for infection, cervical and uterine pathology. Amenorrhea occurs in 50% of women after 1 year of use, increasing to 70% with continued use. DMPA may additionally help with heavy menstrual bleeding, dysmenorrhea due to endometriosis, anemia, bothersome perimenopausal symptoms, Sickle cell disease or be used in combination with anticoagulants or anticonvulsants [3]. While studies regarding associated weight gain are mixed, this concern may limit some women's choice of DMPA.

Bone mineral density (BMD) decreases while using DMPA but BMD loss reverses after discontinuation [6]. Long-term fracture and osteoporosis risk after DMPA use is unknown. The Federal Drug Administration (FDA) recommends that DMPA not be used long-term in women unless other forms of contraception are not adequate [2]. Depot medroxyprogesterone can be used with a history of uncomplicated VTE but in women with risk factors for arterial cardiovascular disease (smoking, older age, diabetes, poorly controlled hypertension, known vascular disease, history CVA, and current VTE), DMPA should be avoided [2]. Studies show the prevalence of endometrial cancer decreased among DMPA users and, theoretically, ovarian cancer may be reduced given DMPA's prolonged ovarian suppression [7].

LARCs: Intrauterine devices

Intrauterine devices (IUDs) are long acting, rapidly reversible, highly effective, safe and gaining popularity among all-aged women [8,9]. Continuation rates are higher among IUD users than in those using DMPA or ECCs [8]. Pelvic inflammatory disease (PID) risk is less than 1% with no increased risk of acquiring Human Immunodeficiency (HIV) or Human Papilloma Virus (HPV). Ectopic pregnancy risk in IUD users is low, but needs to be excluded if pregnancy occurs. The copper IUD (TCu 380A) creates a cytotoxic inflammatory response in the endometrium impairing sperm migration, viability and implantation [8]. The levonorgestrel (LNg) IUDs thicken cervical mucous, cause endometrial suppression and

impair implantation with variable effect on ovulation due to low plasma levels. The TCu 380A is recommended to be replaced every 10 years but may be left in place for 12 years in women over 25.

The copper IUD may initially cause heavier and more painful menses, with both improved after 6 months and treatable with non-steroidal anti-inflammatory drugs (NSAIDs). It is the only IUD recommended for emergency contraception and should be inserted within 120 hours of unprotected intercourse. The LNg IUDs range from 13.5 mg to 52 mg in dosage, with the low dose IUD maintaining menstrual cyclicity and the higher dose IUDs potentially causing amenorrhea. The LNg IUDs benefit heavy menses, dysmenorrhea, endometriosis-related pelvic pain, adenomyosis, and endometrial intraepithelial neoplasia (hyperplasia) [3,8]. Changing out LNg IUDs is recommended at 3-5 years but it is feasible to extend use of higher dose LNg IUDs to 7 years in older premenopausal women [8]. Backup contraception is recommended for 5-7 days after LNg IUD placement. Prolonged or unscheduled bleeding is common for 4-6 months with light menses generally thereafter [8]. IUDs can be used in adolescents and nulliparous women with placement eased by NSAIDs and paracervical anesthesia [9]. Perforation rates occurring at time of placement are 1/1000 with expulsion rates 2-10% [8]. Contraindications to IUDs include suspected pregnancy, acute PID, bicornuate uterus, cervical stenosis, markedly distorted cavity due to leiomyoma, and Wilson's disease or copper allergy (TCu 380A). Abnormal bleeding should be evaluated prior to IUD placement for infection and cervical or endometrial pathology.

Special Circumstances: In women with current or past breast cancer, the TCu 380 is favored over the LNg IUDs [2,8]. For women without a history of breast cancer, the data is conflicting regarding the risk of developing breast cancer while using LNg IUDs [10]. In women with a history of liver carcinoma, the TCu 380A is recommended over LNg IUDs [2]. In women with HIV, IUDs are safe and do not increase risk of transmission or drug interactions with antiretroviral therapy. There is limited data regarding the safety and efficacy of IUDs with immunosuppression unrelated to HIV, but available studies do not report higher infection rates [11]. The advantages of both types of IUDs outweigh the risks for women with uncomplicated solid organ transplants [2]. For improved compliance, IUD placement can occur immediately after birth and placental delivery with expulsion rates 10-40%, infection rates 0-11% and perforation rates 1% [8]. The LNg IUDs may initially have associated emotional lability, weight gain and depression, most of which improve. Women with IUDs can safely undergo magnetic resonance imaging (MRI). IUDs can be removed at ages 52-55 or LNg IUDs can remain in place for women desiring postmenopausal estrogen therapy.

LARC: Subdermal implant

The etonogestrel implant (EI), a single-rod progestin, is easily placed, highly reliable and rapidly reversible [8]. The EI is highly effective due to inhibition of gonadotrophin secretion, follicular maturation and ovulation. While contraception is its only approved indication, it appears promising for endometriosis-related pain. The EI contains 68 mg of etonogestrel, with slowly declining serum levels adequate to maintain contraceptive effect over 5 years [8]. The manufacturer recommends replacing EI every 3 years. It is not contraindicated in obesity, but its effectiveness in women with BMIs greater than 30 kg/m² has not been well studied [2,8]. Most women are candidates for EI with standard contraindications including pregnancy, current or past history VTE, hepatic tumor or active liver disease,

undiagnosed abnormal uterine bleeding, history of breast cancer and sensitivity to any component of the method.

Epidemiologic studies have not identified an increased risk of CVA, myocardial infarction or VTE in users of progestin-only OCs and thus, the CDC has indicated progestin only contraceptives may be a reasonable choice for women with a history of VTE [2]. Contraceptive effect with EI may be decreased with use of antiretroviral medications, anticonvulsants, and immunosuppressives as mycophenolate mofetil, modafinil and protease inhibitors [2]. For these women, other LARCs or contraceptive options are more ideal. The most common side effect of EI is unscheduled bleeding, which often decreases 3-6 months after insertion but can persist through 3 years of use [8]. Discontinuation rates are up to 15% due to unscheduled bleeding, especially persisting greater than ½ days of a 90-day reference point. Successful treatment for unscheduled bleeding with EI has been short course NSAIDs, doxycycline, an ECC or supplemental low dose estrogen. Other adverse effects include headache, weight gain, acne, breast tenderness, mood lability and abdominal pain [8]. The EI does not induce bone loss as seen with DMPA. It does not have significant effect on lipid metabolism or liver function. When pregnancy is reasonably excluded, insertion (and removal) of EI is well tolerated and easily performed by clinicians who have undergone a certified training course. A back-up method for 5-7 days is recommended after initial placement.

Barrier Methods

Diaphragm, cervical cap, sponge and condoms

For women desiring hormonal free options, barrier methods provide safe, immediately available, reversible and affordable contraception [2]. Diaphragms and cervical caps (failure rates 14-29% in first year of use) require self-motivation, do not protect against sexually transmitted infections (STIs), have been linked with urinary infections (UTIs) and vaginal irritation, may be difficult to place especially with pelvic relaxation and need to be refitted after pregnancy [2,12]. Nonoxynol-9 spermicide can cause irritation, burning, itching or rash. Diaphragms, made of silicone, come in variable sizes (65-80 mm diaphragms fit most women), and are designed to be used with spermicide gel [2]. Each new episode of intercourse should be preceded by insertion of fresh spermicide and diaphragms removed by 24 hours after placement. Silicone cervical caps come in 3 sizes (22, 26 and 30 mm) to be used for women never pregnant, women who have undergone abortions or cesarean sections, and vaginally delivered women, respectively [12]. Cervical caps are meant to be used with spermicide and should be removed by 48-72 hours after placement to avoid the small risk of toxic shock syndrome [2].

Diaphragms and cervical caps are by prescription. Sponge contraception (one time use) is a 2 inch foam disk moistened prior to placement to activate Nonoxynol-9 within the sponge. It can be inserted intravaginally up to 24 hours before intercourse and not worn greater than 30 hours [13]. Spermicides are available in cream, film, foam, gel or suppositories. Maternal use of spermicide has not been linked to fetal anomalies [2]. Male condoms are readily accessible with effectiveness (2-18% failure rates yearly) based on self-motivation, placement prior to any genital contact and removal only after completed intercourse [2,12]. Most condoms are latex, protective from STIs and should be used with water-based or silicone lubricants. Natural membrane condoms have small pores which may increase the risk of STIs, especially HIV.

Synthetic condoms can be used in couples allergic or sensitive to latex [2]. Condom breakage and slippage during intercourse are each a 2% risk. Education in proper use of condoms is important to maximize effectiveness. The female condom (5-21% pregnancy rates), available by prescription in the U.S., is a soft, loose fitting synthetic latex or nitrile sheath lined with a silicone lubricant. It can be placed before intercourse and does not need to be removed immediately after ejaculation. It can be used with other methods of contraception but should not be used for anal intercourse.

Emergency contraception

Women and their partners should have available emergency contraception (EC). The TCu 380A IUD is the most effective EC (failure rate 0.2%), followed by ulipristal acetate (by prescription, failure rate 1.4%) and levonorgestrel (1.5 mg orally as Plan B One-Step available over the counter, failure rate 2-3%) [2,14]. The latter two methods work primarily by delaying ovulation. Variables affecting EC include BMI, conception probability based on day of cycle and further intercourse after EC.

The TCu 380A provides continuing contraception and should be placed within 5 days of unprotected intercourse [15]. Levonorgestrel should be taken within 72 hours of unprotected intercourse and ulipristal, a selective progesterone receptor modulator, within 5 days of sex. Testing should be done if pregnancy is suspected as ulipristal and TCu 380A can adversely affect an established pregnancy. Efficacy of oral EC may be affected by anticonvulsants, antituberculosis drugs, antiretrovirals, antifungals and St. John's Wort [2]. Progestin only OCs should not be used with ulipristal or within 5 days of its use. Contraception should be started after oral EC and further intercourse discouraged until efficacy established. If vomiting occurs with oral EC, the TCu 380A IUD can be offered.

Sterilization

Female sterilization (or tubal ligation, TL) is the most common method of contraception worldwide (19%); in the U.S., 16% of women ages 15-44 rely on sterilization [2,15]. Vasectomy appears the safest method of permanent sterilization. Regret following sterilization includes young age, nonwhite race, marital status, postpartum timing for sterilization and insurance status. Tubal ligation can be done immediately postpartum (by Pomeroy, modified Pomeroy or Parkland surgical methods) or done later by laparoscopy or hysteroscopic sterilization, depending on patient preference and surgical risk factors [15]. Entire tubal removal or bilateral salpingectomy is becoming more common given recent data showing reduced risk of ovarian cancer after salpingectomy. Female sterilization is not associated with an increase in subsequent menstrual bleeding or dysmenorrhea [15]. There is no impact of sterilization on sexual function, ovarian reserve or an increased incidence of breast cancer.

Conclusion

There are many effective, well-tolerated, safe and rapidly reversible contraceptive choices. The long-acting, reversible contraceptives, as the IUDs and sub dermal implant, are gaining popularity based on their ease of use and reliability. The LARCs and other highly effective contraceptives offer women the ability to meet their reproductive goals. For some women, hormonal options are less ideal and other non-hormonal methods are available. Clinicians and patients should regularly discuss best choice contraception for individual needs.

Fortunately, many options additionally offer benefit for heavy menstrual bleeding, dysmenorrhea, chronic pelvic pain and other gynecological issues.

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