Examining the use of oral contraceptives in the management of acne

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Abstract: Combined oral contraceptive pills (cOCPs) are often used in the treatment of acne in females. They are effective, safe, and easy to use in appropriate patients in combination with more conventional acne therapies. This article will briefly address the physiologic rationale for the use of cOCPs in the treatment of acne. It will also review efficacy by examining relevant clinical trials. Safety considerations and the adverse event profile for oral contraceptives will be presented. Finally, practical considerations for prescribing cOCPs will be discussed.

Keywords: oral contraceptives, acne, treatment

Introduction

Acne is a problem for women in all age groups. It generally begins at adrenarche, between the ages of 8 and 10 years, and peaks around age 17. Studies have shown that 100% of females are affected sometime during their adolescent years.¹ While often considered a side effect of puberty, adult acne is also fairly common, occurring in 5% to 12% of adult women. Surprisingly, it can continue to be a problem for some women even into their postmenopausal years.

The psychosocial impact of acne is undeniable; adversely impacting the quality of life of those affected. Studies have shown that the level of impairment is similar to that seen in arthritis, back pain, diabetes, asthma, and epilepsy.² Adults with severe acne have decreased employment rates compared to their unaffected peers.³ In addition to the psychological toll, acne can lead to permanent scarring and result in significant, life-long disfigurement.

Therefore, effective use of all available acne treatments is paramount to gaining control of this disorder and helping those affected. While excellent treatments are available, acne in females can pose a unique challenge for the treating physician. It is often recalcitrant to conventional acne therapies, including systemic antibiotics and even isotretinoin. Combined oral contraceptives and other hormonally targeted treatments can be effective in this group of patients and should be considered in the treatment plan for females with acne. Their use will be reviewed in this article.

Physiology/basic science rationale Acne physiology

Four major processes are felt to play a role in the pathogenesis of acne: 1) Follicular hyperkeratinization contributes to the formation of a primary acne lesion, the comedone. This hyperkeratinization causes follicular plugging which then entraps the follicles

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contents, including sebum and bacteria. 2) Increased sebum production results in extension of the follicular unit and assists with plug formation. 3) Comedone rupture initiates an inflammatory cascade in the surrounding tissues resulting in the recruitment of immune cells and the formation of inflammatory papules, pustules and nodules. 4) *Propionibacterium acnes*, bacteria present on the skin surface and within follicular units, thrives in this environment, and contributes to the inflammatory cascade through its activation of toll-like receptor 2 (TLR2) and other mediators.⁴

Different acne treatments target these different, yet entwined processes. For instance, benzoyl peroxide is bactericidal against *P. acnes*. Salicylic acid and topical retinoids are comedolytic and decrease follicular hyperkeratinization. Topical retinoids also decrease TLR-2 expression.⁵ Antibiotics play both an anti-inflammatory role and are bactiostatic against *P. acnes*. Hormonal therapies, like combined oral contraceptive pills (cOCPs), target sebum production and may also play a role in decreasing follicular hyperkeratinization.⁶⁻⁸ Oral isotretinoin is the only medication that exerts action against all four of the steps, but its mechanism of action has not been fully elucidated.

Sebum production is upregulated during physiologic and pathologic states of increased androgen production and acne is seen in these conditions. In women, androgens are produced primarily by the ovaries and adrenal glands. Acne typically begins during adrenarche, when the adrenal gland begins to produce large quantities of dehydroepiandrosterone (DHEAS). Acne also develops in conditions of androgen excess; including polycystic ovarian syndrome, adrenal and ovarian tumors, and congenital adrenal hyperplasia. Administration of testosterone, dehydroepiandrosterone, and androstenedione have been shown to increase sebum production and the size of sebaceous glands.^{9,10} Acne flares are also seen during periods of stress, which is also a state of increased adrenal androgens. Interestingly, castrated male patients, those without testicular androgens, and those with androgen receptor defects are not afflicted with acne.¹¹

Most females with acne will have circulating androgen levels within the normal range. However, studies have shown that as a group, females with acne trend towards the higher end of normal.¹² It may also be that androgen metabolism is increased at the level of the pilosebaceous unit as well, either independently or dependently on the level of circulating androgens. Androgen receptors have been localized to the outer root sheath of keratinocytes and to the basal layer of the sebaceous gland.^{13,14} Androgens are thought to stimulate

growth and differentiation of sebaceous glands. The exact molecular mechanisms are yet to be elucidated.

How do oral contraceptives work?

cOCPs include an estrogen component, usually ethinyl estradiol, and a progestin component which will vary. Estrogens are known to decrease sebum production. They are hypothesized to accomplish this in several ways, both locally at the level of the sebaceous gland, and systemically.¹⁵ First, they may directly oppose androgens at the local level and regulate genes involved in sebum production and sebaceous gland growth.¹⁵ Second, they provide negative feedback on the pituitary/hypothalamus. That is, they inhibit the anterior pituitary's production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), thus decreasing ovarian production of the androgen, testosterone. Third, estrogen administration increases sex hormone binding globulin, which binds serum testosterone, decreasing the amount of free testosterone available to bind with the androgen receptor.¹⁵ The efficacy of cOCPs in the treatment of acne is felt to be secondary to these estrogenic effects. Ethinyl estradiol is the estrogen in most oral contraceptives and comes in various dosages and dosing regimens. First-generation oral contraceptives had higher doses of ethinyl estradiol, around 0.1 mg. Newer formulations contain much lower doses of estrogen, typically 0.020 to 0.035 mg, which minimize the adverse effects that can be associated with estrogen use. These lower dose estrogens still maintain the ability to suppress sebum production.

Use of estrogen has several safety issues, including: increased cardiovascular disease and hypercoagulability, and an increased risk of endometrial and breast cancers. To minimize the risk, most cOCPs include a combination of an estrogen with a progestin. Synthetic progestins act at the progesterone receptor but also react with the androgen receptor to varying degrees and thus may potentiate acne. They can also cause glucose intolerance and interfere with the effect of estrogen on sex-hormone binding globulin. Older synthetic progestins like the first-generation gonane, norethindrone, and the second-generation estranes, norgestrel and levonorgestrel, were derived from progesterone. In vitro studies suggest that these progestins may cross-react with the androgen receptor.¹⁶ Newer synthetic progestins, like the third-generation gonanes, desogestrel and norgestimate, have less activity at the androgen receptor and more specificity for the progestin receptor, thus the androgenic effects are minimized. Drospirenone is a relatively new fourth-generation progestin with a pharmacologic profile that is more similar to progesterone. It blocks

endogenous androgens from binding the androgen receptor and is thus anti-androgenic. Drospirinone is an analogue of spironolactone, a diuretic with anti-mineralocorticoid activity and anti-androgen activity also used in the treatment of acne. Drospirinone's anti-mineralocorticoid properties may help to counteract the bloating and water retention produced by estrogen in the cOCPs. Multiphasic cOCPs with varying progestin levels were designed to minimize androgenic effects by decreasing the overall amount of progestin delivered over the course of the cycle. They start with lower progestin levels and increase to provide the higher androgen dose at the end of the menstrual cycle, which more closely mimics physiology.¹⁷ Fortunately, in all cOCPs, the effects of the estrogen outweigh the effects of the progestin and therefore the overall effect is a decrease in androgen levels and improvement in acne.

Efficacy

Clinical trials have shown that cOCPs are effective in the treatment of acne. Changes in lesion counts, physician global assessments, and patient satisfaction have generally been the outcome measures of these studies. Though many cOCPs have shown efficacy in the treatment of acne in clinical trials, and all are hypothesized to work through their estrogenic effects, only 3 oral contraceptives have been approved by the FDA in the United States for use in patients with acne who desire contraception. These include: norgestimate 0.180 mg/0.215 mg/0.25 mg ethinyl estradiol 0.035 mg (Ortho-TriCyclen®; Ortho-McNeil-Janssen Pharmaceuticals, Inc.), norethindrone 1 mg ethinyl estradiol 0.020 mg/0.030 mg/0.035 mg (Estrostep®; Warner Chilcott), and drospirenone 3 mg ethinyl estradiol 0.02 mg (YAZ®; Bayer HealthCare). Cyproterone acetate (Diane®, Dianette®) is a synthetic derivative of 17-hydroxyprogesterone, approved in Europe for the treatment of acne, hirsutism and alopecia, but is not available in the United States. It may be used as a sole agent or in combination with ethinyl estradiol. While few are approved for the use in acne, clinical trials suggest that many other oral contraceptives are also effective. Those with ethinyl estradiol and levonorgestrel, desogesterel, norgestimate, gestodene, norethindrone acetate, chlormadinone acetate, drospirenone, cyproterone acetate, all have demonstrated efficacy in the treatment of acne.

A recent Cochrane review provided a comprehensive assessment of the efficacy of cOCPs for the treatment of acne in women.¹⁸ This review looked at all randomized controlled clinical trials which compared any combined cOCP to either a second cOCP, oral antibiotic, topical acne treatment, no treatment or placebo. Included studies

were required to assess at least one of the following measurements: change in specific lesion types, change in total lesion counts, physician or patient global assessment, psychosocial function outcome, and early discontinuation secondary to adverse events, including worsening of acne. A total of 81 trials were identified with 23 trials (a total of 7162 patients) meeting inclusion criteria. Metanalysis revealed the following conclusions: cOCPs reduced inflammatory and non-inflammatory lesion counts, resulted in decreased acne severity grades, and improved patients' self assessment of acne in all of the trials comparing oral contraceptives to placebo. In most of the studies analyzed, total acne lesion counts decreased 40% to 60% with cOCP use, while an approximate 30% reduction in total lesion counts was seen in placebo groups. Typically, inflammatory lesion counts show greater improvement than noninflammatory lesion counts. Studies comparing oral contraceptives did not convincingly show superiority of one oral contraceptive to another in the treatment of acne. cOCPs containing chlormadinone acetate or cyproterone acetate seemed to improve acne better than those containing levonorgestrel; however, this was based on limited clinical data. Discontinuation secondary to adverse events also did not vary between cOCPs. There were not enough trials to reach a conclusion about cOCPs versus oral antibiotics. Nor were there head to head studies comparing topical acne treatments with cOCPs deemed adequate enough to include in the review. Compilation of evidence was difficult due to variable study designs. More research needs to be done to draw conclusions about the comparative efficacy of different cOCPs.

Safety

There are several important safety concerns and interactions to consider when starting a patient on oral contraceptives. More serious adverse events may occur in certain patients and should thus be avoided in those at risk (Table 1). All patients starting on cOCPs for acne should be thoroughly vetted regarding risk factors, with particular focus on lifestyle choices and family history. Patients should be routinely counseled about possible side effects from cOCP use and asked about the development of any side effects at their follow-up appointments.

Hormonal changes lead to the most common side effects. Nausea, breast tenderness, headache, and bloating are attributed to the estrogen component of the cOCP. Fatigue, irritability, weight gain, acne, oily skin, increased low-density lipoprotein level (LDL) and breast tenderness are attributed

Table I Contraindications to oral contraceptive use

Smokers greater than 35 years old	Morbid obesity
Undiagnosed abnormal uterine bleeding	Estrogen dependent neoplasms, breast cancer, endometrial cancer, hepatic adenomas and carcinomas
Pregnancy and lactation	History of jaundice in pregnancy or with prior OCP use
Thromboembolic disease	Hypersensitivity
Hypercoagulable states	Migraine headaches after age 35 or before age 35 with focal neurologic deficits/aura
Cardiovascular disease including poorly controlled hypertension, angina, complicated valvular disease	Diabetes with evidence of nephropathy, retinopathy, neuropathy, vascular disease or >20 years duration
Hypertriglyceridemia	Severe cirrhosis

to the progestin component of the cOCP. Decreased libido is also attributed to low progesterone levels.

Menstrual irregularity can also occur. As the levels of estrogen in cOCPs has decreased, the incidence of unscheduled bleeding and spotting has increased. If estrogen levels are too low, hypomenorrhea and early cycle breakthrough bleeding can occur. If progesterone levels are low, late cycle breakthrough bleeding results. Knowledge of these effects can help the clinician choose the right cOCP for their patient and troubleshoot any problems with ongoing cOCP therapy.

cOCPs now carry a black box warning regarding their risk of cardiovascular events, including venous thromboembolism (VTE). The greatest risk for VTE occurs within the first year of use and among carriers of thrombogenic mutations.¹⁹ The WHO Medical Eligibility Criteria for Contraceptive Use advises that the risks of cOCP use may outweigh the benefits in women with known thrombophilias.²⁰ Examples of such thrombophilias include: factor V Leiden deficiency, protein C and protein S deficiencies, antithrombin III deficiency, dysfibrinogenemia, prothrombin 20210, hyperhomocysteinemia, resistance to activated protein C, and high levels of factor VII and von Willebrand factor. Women with factor V Leiden deficiency who use cOCPs have a 35-fold increase risk of developing VTE over their baseline risk. Depending on whether they are heterozygous or homozygous, the increase in risk ranges from 4- to 10-fold, to 50- to 100-fold, respectively.²¹ Other factors that increase risk for VTE in women taking cOCPs include: age greater than 45, smoking greater than 10 cigarettes per day, and personal history of VTE.^{22–24} A personal and family history query to evaluate risk factors for VTE and cardiovascular disease and baseline blood pressure and body mass index should be performed prior to starting cOCPs. Although a serious potential side effect, the incidence of VTE is rare, and routine screening of asymptomatic women without a family history of thrombophilia is not recommended.²⁵

Both the amount of estrogen and type of progestin play a role in VTE. There is reduced risk with lower amounts

of ethinyl estradiol.²⁶ Recently, there has been concern that certain progestins may increase this risk. Drospirenone and cyproterone, which both have antiandrogen activity, have been suggested to carry a greater risk of VTE.^{27,28} While there have been no randomized controlled trials, case control studies and a cohort analysis suggest that cyproterone may carry up to a four-fold increased risk.^{29,30} However, the European Active Surveillance, a large prospective, controlled, multinational cohort study of new users of drospirenone, and other progestin containing oral contraceptives, reported similar rates and identical hazard ratios for venous thromboembolism in users of drospirenone containing cOCPs versus others.³¹

Users of cOCPs do carry a risk of developing hypertension; therefore blood pressure should also be monitored during follow-up visits. Other cardiovascular events that have evidence for association/risk include: arterial thromboembolism, cerebral hemorrhage and thrombosis, mesenteric thrombosis, and myocardial infarction. There is also evidence for association/risk for the development of gallbladder disease, hepatic adenomas and other benign liver tumors, and retinal thrombosis in patients taking cOCPs. There are many other reactions that patients may experience that are considered related to the use of cOCPs. Leg edema and varicose vein aggravation are additional cardiovascular risks. Neurologic side effects include: depression, migraine, mood changes, and worsening chorea. Dermatologic effects include chloasma, melasma, and other rare dermatoses. Nausea, vomiting, abdominal pain and cramping, appetite changes, bloating, cholestatic jaundice, and focal nodular hyperplasia are additional gastrointestinal and hepatic adverse events. Genitourinary side effects include: cervical ectropion, cervical secretions, endocervical hyperplasia, fibroid enlargement, vaginal candidiasis and vaginitis. cOCP use may cause exacerbation of porphyria, and decrease folate levels. Rhinitis might also occur with their use. Ophthalmologic side effects include contact lens intolerance, and change in corneal curvature. Anaphylactic and anaphylactoid reactions may also occur.

Use of cOCs containing the progestin, drospirinone, may also result in an increase in serum potassium levels. Monitoring of potassium levels should be done in patients with underlying kidney disease, or those taking medications that can increase serum potassium levels, such as nonsteroidal anti-inflammatory agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, aldosterone antagonists, and heparin. Also, acne patients treated with spironolactone in combination with a drospirinone containing cOCP should be closely monitored for excessive potassium levels.

Oral contraceptives and oral tetracyclines are commonly used together in the treatment of acne. Backup contraception for patients using these medications concomitantly is routinely recommended by pharmacists. The mechanism of interference may be due to an alteration of the bacterial flora resulting in the impaired absorption of estrogens. However, in patients taking doxycycline and tetracycline, studies have shown that estrogen levels are unaffected.^{32,33} While there have been case reports of pregnancy occurring on such combinations, pregnancy rates were no greater than those from failure rates reported from the cOCP alone.^{34,35} Individual variations in estrogen metabolism likely explain oral contraceptive failure.³⁶ However, what additional impact the use of oral antibiotics has on those individuals needs to be further studied. Currently, there are no pharmacokinetic data or randomized controlled clinical trials supporting that oral antibiotics decrease the efficacy of oral contraceptives, with the notable exception of anti-tuberculosis drugs like rifampin.³²

If the onset of acne in females is acute and severe, or if the acne is accompanied by signs of hyperandrogenism, investigations should be performed to rule out an underlying

endocrine abnormality. A complete medical history and physical examination should be performed in these patients looking for signs of hyperandrogenism. These signs include: irregular menstrual periods, obesity, hypertrichosis, female pattern alopecia, clitoromegaly, and deepening of the voice. An appropriate minimum laboratory workup includes drawing serum total testosterone, free testosterone, and DHEAS. Some also advocate drawing LH and FSH. These should be performed during the luteal phase of the menstrual cycle and women should be off oral contraceptives for at least one month prior. If DHEAS is elevated, the adrenal gland is the source of the excess androgens. DHEAS levels greater than 8000 ng/dL are indicative of a possible adrenal tumor. DHEAS levels between 4000 and 8000 ng/dL may indicate the presence of congenital adrenal hyperplasia. If testosterone levels are elevated, while DHEAS levels remain normal, the ovaries are the source of excess androgens. If the total testosterone is greater than 150 to 200 ng/dL an ovarian tumor may be the source. Mild elevations in total testosterone may be indicative of polycystic ovarian syndrome. An increased ratio of LH to FSH is also indicative of this. Patients identified with abnormalities should be appropriately referred to specialists.

Another question that practitioners often ask when starting oral contraceptives is when to initiate Papanicolaou smear screening for cervical cancer prevention, especially in adolescents. The current recommendation of the American College of Obstetricians and Gynecologists written in 2003 is as follows: cervical cancer screening should begin within 3 years after first vaginal intercourse or by age 21, whichever comes first. Guidelines for subsequent screening vary based on age, type of screening test, and prior test results. Physicians prescribing oral contraceptives should routinely ask their

Table 2 Starting oral contraceptives

	First day start	Sunday start	Quick start
When to take 1st pill	Started on first day of menses	Started on the first Sunday after the onset of menses	Started anytime during the menstrual cycle after a negative urine pregnancy test
Back-up contraception	Back-up contraception not needed but advocated by some for the first week	If Sunday falls on days 1–5 of menses: back-up contraception advocated for the first week If Sunday falls on days 6–7 of menses: back-up contraception needed for the first month	Back-up contraception needed for the first month
Advantages	Less chance of pregnancy occurring during first month	Easier pill administration- most packets of pills labeled with day of the week	Better patient compliance
Disadvantages	Poorer patient compliance	Poorer patient compliance	Possibility of pregnancy occurring during first month, despite negative initial testing

patients about their sexual activity and refer their patients to a gynecologist or primary care provider when appropriate.

Practical management tips

How to start oral contraceptives

cOCs may be started in three different ways (Table 2). They may be started on the first day of the patient's menstrual period, within 24 hours of the period commencing. This is known as "First Day Start" method. The theoretical advantage to this method is that there is no need for backup contraception. Despite this, however, many practitioners still instruct their patients to use backup contraception for the first week.

In the "Sunday Start" method, the first pill is taken on the Sunday following the first day of the last menstrual period. Backup contraception should be used for the first week if it is started between days 1 and 5 of menses. If Sunday falls beyond day 5, backup contraception should be used for the entire first month.

In the "Quick Start" method, cOCs may be started at any time during the menstrual cycle. This has been shown to increase compliance. In this method, a urine pregnancy test is drawn in the office and, if negative, the patient may begin taking the cOCs immediately. Some practitioners have their patients take their first pill in the office to increase compliance.³⁷ Patients should use a backup form of contraception for the first month when using the "Quick Start" method. Fear of undiagnosed pregnancy is a barrier to physician prescription of cOCs. Physicians may delay pill initiation until the patient's next period if they have engaged in unprotected intercourse, in fear of teratogenicity. Although cOCs carry a pregnancy category rating X, according to current literature, exposure to oral contraceptives during early pregnancy is not teratogenic or dangerous to pregnancy.^{38,39} There is no association between genital and nongenital malformations and the use of low dose oral contraceptives during early pregnancy.⁴⁰⁻⁴² If pregnancy does occur in a patient using the "Quick Start" method, the pregnancy is easily diagnosed after the patient does not experience withdrawal bleeding during the placebo cycle of her oral contraceptive pack.^{43,44} The use of cOCs in pregnancy for the treatment of acne is obviously contraindicated.

Spotting/breakthrough bleeding and how to manage

Spotting and breakthrough bleeding may be a problem for women started on oral contraceptives. Spotting is defined as

bleeding not requiring sanitary protection while breakthrough bleeding requires the use of a tampon or menstrual pad. Up to 20% of women stop using oral contraceptives secondary to this side effect.⁴⁵ Spotting and breakthrough bleeding are common in the first 3 to 4 months after starting oral contraceptives and patients should be counseled regarding this side effect. After this period, it tends to cease. Both the amount of estrogen and progestin and the type of progestin can contribute to breakthrough bleeding. Estrogen causes uterine lining proliferation and progesterone stabilizes the uterine lining. Too little estrogen or too little progesterone can lead to spotting and breakthrough bleeding. Early cycle bleeding is thought to be secondary to low estrogen and late cycle bleeding to low progesterone. cOCs with the same amount of estrogen, but different types of progestins, also have significant differences in spotting and breakthrough bleeding.⁴⁶ The choice of progestin is thus important. The estrogen to progesterone ratio is also important. In studies where the ratio of estrogen to progesterone was maintained but the concentrations varied, preservation of the ratio was associated with acceptable levels of breakthrough bleeding.⁴⁷

cOCs are available as monophasic, biphasic, triphasic, extended cycle, and continuous use preparations. Extended cycle and continuous use preparations, which allow for less withdrawal bleeds, have the highest incidence of breakthrough bleeding. Biphasic and triphasic cOCs were designed to lower the amount of hormones in cOCs without increasing the incidence of breakthrough bleeding, and possibly decrease this incidence, though evidence has been insufficient to support this.⁴⁸

Other factors that may contribute to breakthrough bleeding include: lack of adherence, smoking, and medication interactions. For example, skipping a pill or failing to take a pill at the same time each day can lead to spotting. In patients who smoke, the habit decreases the estrogenic effectiveness of the pill. This is felt to be secondary to the induction of hepatic estrogen and also progesterone metabolism by cigarette smoking.^{49,50} Smokers have higher rates of menstrual irregularities and more breakthrough bleeding.⁵¹ Also, certain prescription and OTC medications, particularly those that induce the cytochrome P450 system, can cause breakthrough bleeding and can cause contraceptive failure. Examples of common P450 inducers include: rifampin, isoniazid, dexamethasone, griseofulvin, anticonvulsants and alcohol, though the list is more extensive. Pathologic causes of intermenstrual bleeding may mimic breakthrough bleeding and spotting and should be ruled out. For example, uterine or

Table 3 Strategies for managing breakthrough bleeding^a

Early breakthrough bleeding or spotting	Late breakthrough bleeding or spotting
Secondary to low estrogen	Secondary to low progesterone
Treat with supplemental estrogen: Estrogen 1.25 mg/day or estradiol 2 mg/day $\times$ 7 days	Change to a cOCP with a more androgenic progestin or higher amount of progestin
or	or
Change to a cOCP with a higher concentration of ethinyl estradiol	Switch from a multiphasic to a monophasic cOCP

^aFirst, rule out lack of adherence, smoking, medication effect, and pathologic bleeding.

cervical malignancy and cervicitis from sexually transmitted diseases may cause bleeding between menstrual periods. If bleeding extends beyond 4 months, or begins after a patient has been on a cOCPs for several months without bleeding, an investigation is warranted.⁵²

Strategies for managing breakthrough bleeding are as follows and summarized in Table 3. First, rule out lack of adherence, smoking, and medication effects by taking a good history. Pathologic processes, as noted above, that may be causing unexpected bleeding should be considered. Next, it should be determined when during the cycle the breakthrough bleeding or spotting occurs. If it is early in the cycle, supplementation with estrogen may be helpful. Estrogen 1.25 mg/day or estradiol 2 mg/day may be given for 7 days when bleeding occurs.⁵² This may be repeated if necessary. However, changing the oral contraceptive to one with a greater amount of ethinyl estradiol may also help and be a more permanent solution. This may be particularly helpful for women taking cOCPs with low doses of ethinyl estradiol ($<35 \mu\text{g}$). If breakthrough bleeding occurs late in the cycle, changing the oral contraceptive to one with a higher concentration, or more androgenic type of progestin, may be beneficial. Switching from a multiphasic to a monophasic pill may also solve the problem as it allows for a steady dosing of progestin. Of utmost importance is managing patient's expectations up front by educating patients about this potential side effect.

Conclusion

Several combined oral contraceptive preparations have proven to be effective and safe in the treatment for acne in women when used appropriately. All of those approved for use in acne, and many others, have near equal efficacy in decreasing total acne lesion counts, with a greater effect on inflammatory acne. Their use should regularly be considered in female patients with acne, especially those not responding to first line treatments, namely topical therapies and oral

antibiotics. Careful screening and selection of patients is important to minimize risk. Understanding relevant safety concerns with a focus on patient risk factors, including hypertension, smoking and thrombophilias, will help minimize adverse events. In addition, a working knowledge of the individual combined oral contraceptive formulations can help the prescriber to select the best medication for their patient and help with troubleshooting when problems arise. With this knowledge, any physician who regularly treats acne can safely include cOCPs in their therapeutic armamentarium.

Disclosures

The authors declare no conflicts of interest.

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