CONTRACEPTION

A number of refinements in access to, or use of, hormonal contraception deserve our attention

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A year ago, the US Food and Drug Administration (FDA) granted over-the-counter (OTC) status for Plan B, the levonorgestrel-only emergency contraceptive. In the past few years, we have accumulated data on the general impact of improved access to emergency contraception (EC), as well as evidence of its overall efficacy. We also have another year of experience with the levonorgestrel-releasing intrauterine system (Mirena) and its multiple benefits beyond contraception, and with extended hormonal contraceptive regimens. This article highlights what we know about these three forms of contraception.

Greater access to Plan B leads to increased—and faster—use

Now that Plan B is available OTC to both men and women 18 years and older,[1] several questions are in order:

- What are the effects of this change?
- Does OTC access or provision of the drug in advance reduce condom or oral contraceptive use?
- Does it increase the number of sexual partners or rate of sexually transmitted disease (STD)?
- Does it reduce unintended pregnancy?

To acquire the drug OTC, an adult must ask the pharmacist for it and show proof of age. Even before the FDA approved OTC status, many clinicians gave patients an advance prescription or actual medication so an appointment would be unnecessary in a time of need.

Several randomized trials have found that advance provision of EC not only increases its utilization, but causes it to be used sooner.[2–7] Most of the trials conducted so far have compared advance provision of EC with counseling about EC or a prescription for it. Only one trial has included a pharmacy-access arm, and it was conducted before FDA approval of OTC status.[3] It found that pharmacy access did not increase use of EC, compared with standard access (ie, returning to the clinic when EC was needed). It is too early to tell what effect OTC availability will have on the usage rate, but data so far support the practice of giving the patient a supply of EC rather than just a prescription.

Increased access to EC does not affect regular contraceptive behavior

Multiple studies have shown that advance provision of EC has no significant

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Levonorgestrel pills can be taken both at once and as long as 5 days after intercourse

Prescribing information for levonorgestrel emergency contraception (EC) recommends ingestion of the first 0.75-mg tablet within 72 hours (3 days) of a single act of unprotected intercourse, with the second tablet taken 12 hours after the first.[11] However, data show that levonorgestrel EC can prevent pregnancy up to 5 days after intercourse. In a World Health Organization multicenter randomized trial of various EC regimens, levonorgestrel EC prevented 79% to 84% of expected pregnancies when taken within 1 to 3 days, and 60% to 63% when taken 4 to 5 days after intercourse.[12] Randomized trials have also found that taking both 0.75-mg levonorgestrel pills simultaneously prevents pregnancy as effectively as taking them 12 hours apart.

Levonorgestrel EC prevents or delays ovulation by inhibiting the luteinizing hormone surge during the follicular phase.[13] Secondary mechanisms of contraceptive action include thickening of the cervical mucus; decreased pH level, which immobilizes sperm; and decreased recovery of sperm from the uterus.[14]

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Providing the patient with emergency contraception in advance does not increase the number of sexual partners or rate of STD

effect on the use of regular contraception. Studies have examined the impact of EC on both baseline oral contraceptive usage and condom usage and found no significant change in either among women who used EC during the study.[3–6]

… nor does it cause promiscuity or increase the rate of STD

Multiple studies have demonstrated that advance provision of EC does not increase the number of sexual partners or rate of STD.[3–6] The largest of these studies compared both pharmacy access without a prescription and advance provision of EC to standard access. That study included 2,117 sexually active young women and found no difference in the rate of STD or number of sex partners among the three study groups.[3] Smaller studies comparing advance provision of EC with standard access also found no significant difference in these variables.[8,9]

No evidence of fewer unintended pregnancies—yet

We know that progestin-only EC can reduce unintended pregnancy by almost 90%.[10] However, studies have not yet demonstrated such a decrease in the general population. One reason may be that the two studies that considered unintended pregnancy as a primary outcome[3,9] were too small to detect a difference in pregnancy rates, or it may be that EC was underutilized by women in the studies.

Levonorgestrel intrauterine system has benefits beyond contraception

The levonorgestrel intrauterine system (LNG-IUS) has been shown to significantly decrease blood loss and increase hemoglobin and serum ferritin levels in women with idiopathic menorrhagia.[15] The LNG-IUS reduces blood loss to a greater degree (as much as 96% after 1 year) than do placebo, nonsteroidal anti-inflammatory drugs, antifibrinolytic medication, and oral contraceptives.[16] In one study,[16] the LNG-IUS was the only treatment that reduced menstrual bleeding to less than 80 mL/day—the upper limit of normal.

LNG-IUS compares favorably to endometrial ablation

The LNG-IUS provides nonoperative, local, and minimally invasive treatment of menorrhagia, producing clinical results similar to those of different endometrial ablation methods for dysfunctional uterine bleeding or menorrhagia. The LNG-IUS is comparable to endometrial resection in its reduction of blood loss, patient satisfaction, rate of amenorrhea, and recurrent menorrhagia.[17] It also is equivalent to thermal balloon ablation in its reduction

of bleeding and increased quality of life and hemoglobin level.[18,19] And it produces a higher amenorrhea rate than expectant management after endometrial resection in women with adenomyosis, and averts the need for further procedures, such as hysterectomy and repeat resection.[20]

In many women, LNG-IUS renders hysterectomy unnecessary

In a controlled trial involving 56 women on a waiting list for hysterectomy, 64% of those who received the LNG-IUS and 14% of those in a control group removed themselves from the list at the end of 6 months because they were satisfied with symptom control ($P<.001$).[21] In a trial involving 236 women with menorrhagia randomized to LNG-IUS or hysterectomy, the groups had similar quality-of-life scores at 1 and 5 years of follow-up—and costs associated with the LNG-IUS were significantly lower than those associated with hysterectomy, even after 50 women randomized to the LNG-IUS opted for and underwent hysterectomy.[41]

Consider the LNG-IUS a first-line therapy for symptomatic fibroids

The LNG-IUS continuously decreases fibroid and uterine volume and blood loss and increases ferritin levels over time among women with symptomatic fibroids.[22] It should therefore be routinely considered a first-line therapy for women with fibroids who wish to preserve their childbearing potential.

Endometrial hyperplasia is reduced

The LNG-IUS can prevent and induce regression of endometrial hyperplasia.[23,24] In addition, it reduces bleeding and spotting among women using hormone replacement therapy.[25,26] Studies also suggest it may be beneficial in the treatment of stage I endometrial cancer, although further research into this effect is needed.[27]

Endometriosis-related pain is eased

In a randomized trial comparing the LNG-IUS with a gonadotropin-releasing hormone (GnRH) analogue among women with chronic pelvic pain due to endometriosis, both treatments reduced pain and improved psychological well-being to the same degree—but the LNG-IUS caused no systemic hypoestrogenic symptoms, unlike the GnRH analogue.[28] In a randomized trial comparing the LNG-IUS with expectant management among women who had undergone laparoscopic resection of endometriosis, women in the LNG-IUS arm had significantly decreased recurrent dysmenorrhea.[29]

In addition, the LNG-IUS is effective for as long as 5 years, can be used in conjunction with systemic estrogen, and is an effective contraceptive.

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64% of women who received the LNG-IUS removed themselves from a waiting list for hysterectomy at the end of 6 months

Continuous oral contraceptive regimens: 4 effective options

Oral contraceptives (OCs) can be prescribed for continuous use to achieve a number of different goals[30]:

- decrease the number of placebo days per cycle
- reduce the number of placebo weeks or withdrawal weeks per year
- eliminate withdrawal weeks from the cycle entirely
- reduce the incidence of breakthrough bleeding

The first two options are highly effective and produce shorter and fewer bleeds, and the last option is especially appropriate for women troubled by unscheduled bleeding during continuous OC use. All four options decrease menstrual symptoms.

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Reduce the number of placebo days

Compared with the standard 28-day regimen (21 days of active pills followed by 7 days of placebo), extended regimens significantly reduce ovarian activity and produce smaller follicles and a lower estrogen level.[31,32] Extended regimens may involve fewer days of placebo pills per cycle, or very small amounts of estrogen throughout the withdrawal week of the regimen. These modifications may translate into increased efficacy. In two randomized trials comparing extended regimens with a standard regimen, the extended regimens were highly effective, with a Pearl index of up to 1.29 (1.29 pregnancies for every 100 woman-years of use), and produced shorter withdrawal bleeds.[33,34]

Decrease the number of placebo or withdrawal weeks

The FDA approved the first OC to be packaged for extended use (Seasonale) in 2003. Each pack contains 84 active tablets of ethinyl estradiol (0.03 mg) and levonorgestrel (0.15 mg), followed by seven placebo pills. This highly effective regimen has a failure rate of 0.60 per 100 woman-years.[35] Another extended-use OC (Seasonique) contains 7 days of ethinyl estradiol (10 µg) instead of placebo pills and may, therefore, suppress follicular development to an even greater degree during the withdrawal week.[36]

Extended cycles can be achieved with any monophasic OC in an off-label manner. Simply instruct the patient to take one active tablet for 42 consecutive days (known as "bicycling") or for 63 consecutive days ("tricycling"), followed by 4 to 7 pill-free days.

Unscheduled bleeding with the 63-day regimen appears to be similar to the rate associated with the 21-day regimen.[35] An extended-cycle regimen can be modified according to how often the user wants withdrawal bleeding.

Eliminate the withdrawal week

Perhaps the most radical extended-cycle regimen is continuous use of active pills with no placebo or withdrawal interval. This option is safe and acceptable to women, according to two small randomized trials and two prospective trials, but larger studies are needed to confirm these results.[37–40] Continuous use for 1 year is associated with less bleeding, higher rates of amenorrhea, and similar side effects, compared with conventional regimens.[37,38] Patient acceptance and satisfaction also are high,[39] with most women choosing to keep taking the pill continuously. Lybrel, an OC designed for this purpose, contains 20 µg of ethinyl estradiol and 90 µg of levonorgestrel and is intended to eliminate menses through 1 year of continuous use.

Reduce breakthrough bleeding

For women who experience unscheduled bleeding while taking an OC continuously, one option is to stop taking pills when breakthrough bleeding occurs and initiate a hormone-free interval. This approach was studied in a randomized trial in which women were scheduled to take an OC continuously for 168 days.[40] Women who had persistent unscheduled bleeding for longer than 7 days were randomized to a 3-day hormone-free interval or continuation of the active pills. Those who continued taking active pills had more bleeding over the long term, and a large percentage found it necessary to institute a delayed hormone-free interval.

This option may be particularly useful for women who experience persistent breakthrough bleeding on a continuous regimen.[40] ■

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Extended OC regimens reduce ovarian activity and produce smaller follicles and a lower estrogen level than the standard 28-day regimen

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