



Picking the Perfect Pill

How to Effectively Choose an Oral Contraceptive

By Susan Chamberlain, MD, FRCSC



There are over 20 oral contraceptive (OC) preparations on the Canadian market. With so many choices, it is understandable that many clinicians feel confused when selecting an OC to prescribe to their patients. Questions include: What type of progestin should be used? How much estrogen is enough, or too much? Which is better: monophasic or multiphasic?

This article will discuss oral contraceptives only. There is a range of other contraceptive options that will not be discussed here.

How OCs have evolved

Early in the last century, researchers found that progesterone could suppress ovulation in animals and in humans.¹ The original synthetic progestins were contaminated by estrogen, but when the estrogens were removed cycle control was lost and breakthrough bleeding (BTB) occurred. Thus, the estrogen was maintained and

In this article:

1. How oral contraceptives have evolved.
2. How to select an appropriate formulation for each patient.
3. How to manage common side effects.
4. How to ensure long-term compliance.

the combined oral contraceptive (COC) was born. In 1960, the first COC was introduced in the U.S.

The mechanism of action of the COC involves inhibition of pituitary gonadotropin release by estrogen and progestin, thereby suppressing follicular development and ovulation. Progestin confers additional contraceptive effects by altering cervical mucus and suppressing endometrial development.

Over the years, many different progestin compounds have been synthesized for use in OCs



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Table 1

Progestins and estrogens currently available in Canada

Progestins	Estrogens
Norethindrone	Ethinyl estradiol
Norethindrone acetate	Mestranol
Ethinodrel diacetate	
Levonorgestrel	
Norgestimate	
Desogestrel	
Cyproterone acetate (not marketed as an OC)	

(Table 1). Examining the chemical structures of the sex steroids (estrogen, progesterone and testosterone), it is easy to see how minor alterations in structure leads to cross-reactivity between hormone receptors, which varies the physiologic response referred to as hormonal activity.² The comparative hormonal activities have been studied; for each type of oral contraceptive there are tests of estrogenic activity, progestational activity, and androgenic activity. It must be noted however, that these activities are measured in vitro using animal tissues and therefore, may not reflect the response in the human female. It is difficult to predict hormone effects in vivo as the net activity of a formulation depends on the types of hormone components; the doses; the interaction between components; and an individual's steroid metabolism and target organ response, which are genetically determined.

In the 1990's, the "new progestins" (desogestrel and norgestimate) were marketed in

Canada. These progestins were designed to be more specific to the progesterone receptor and thus be less androgenic than earlier progestins. They have less impact on lipid and carbohydrate metabolism. The clinical importance of this difference is debatable as previous OCs did not dramatically change lipid or insulin profiles in healthy individuals.^{3,4}

There has been a reduction in hormone doses since the first OC's were marketed; current preparations contain 20% of the estrogen and 10% of the progestin dose compared to the original pills.³ This reduction is in response to the serious side effects of high dose estrogens (*i.e.*, stroke, myocardial infarct, thromboembolism) and the nuisance side effects of both estrogens and progestins. The net effect has been a decrease in side effects to the possible detriment of cycle control. Efficacy has been maintained, although theoretically there may be less margin of error. Current formulations have an ideal failure rate of 0.1-1.3/100 woman years^{2,5} but population surveys show an actual failure rate of 5-8/100 woman years.⁵

In addition to decreasing the total hormone dose, another alteration in OC formulations has been to vary the doses within each cycle, thus we have biphasic and triphasic preparations. The advantage is the decrease in progestin dosage, as this component may be more

atherogenic and diabetogenic. Again, the clinical importance of these differences has yet to be demonstrated. Although monophasic pills are widely believed to confer better cycle control, this has not been shown in clinical trials.^{3,6} The only proven advantage of the monophasic preparations is the ease of cycle manipulation for the more sophisticated user or to completely suppress menstruation.

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Table 2

Non-contraceptive benefits of oral contraceptives

- Reduction of menorrhagia and dysmenorrhea
- Reduction of benign breast disease
- Reduction of cancer of the endometrium and ovary
- Positive effect on bone mass
- Treatment of acne and hirsutism

In addition to the combined OC, the progestin-only or “mini-pill” is available. This preparation does not reliably suppress ovulation, with 50% of users continuing to have regular ovulatory cycles, and 35% to 40% having variable follicular development.⁷ This leads to persistent break-through bleeding in one third of users and a high discontinuation rate. This pill is also slightly less effective with a failure rate of 2.3-2.5/100 woman-years and a lower margin of error.²

How to choose an OC

Understanding why there are so many OC choices does not mean knowing which one is the best for our patients. Unfortunately, the literature on OCs can be confusing. Although there are many trials comparing products, there are multiple confounding variables within each trial that limit direct comparison, such as type of progestin used, doses of each component, and method of defining and measuring BTB. In addition, the results of various trials can appear contradictory.

Non-contraceptive benefits of the COC (Table 2) are important determinants of OC use. No difference in non-contraceptive benefits has been demonstrated between formulations.

For most women, any of the low-dose pills (*i.e.*, containing 35 µg or less of ethinylestradiol) is acceptable. However, there are clinical situa-

Table 3

Absolute contraindications to oral contraceptives

- Thrombo-embolic disease
- Cardiovascular or cerebrovascular disease
- Migraines with neurologic features
- Hepatic dysfunction
- Estrogen-dependent neoplasia
- Smokers > 35 years of age
- Uncontrolled hypertension

tions where a specific formulation may be preferred.

When choosing an OC, one must consider the absolute contraindications (Table 3). For these



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Table 4

Side effects of oral contraceptives

Estrogen-related

Nausea
Breast tenderness
Headaches

Progestin-related

Mood/libido changes

Other

Break-through bleeding

women, alternate effective methods of birth control should be sought. If estrogen is the problem, the progestin-only pill may be an option. Relative contraindications to estrogen include migraines without neurologic features, and risk factors for cardiovascular disease, such as smoking, age, hypertension, obesity, and diabetes mellitus. In these patients, the COC with the lowest possible dose of estrogen should be used, although no difference in safety between low-dose pills has been demonstrated.

Women who are breast-feeding require effective contraception. There is anecdotal evidence that the combined OC may affect quality or quantity of milk. The progestin-only pill may be a good option for these women as the contraceptive efficacy may be comparable to the COC in a non-ovulating population. Patients must be advised of the need to switch to a more effective method when weaning.

Women with high androgen states, such as polycystic ovarian syndrome or who suffer from hirsutism or acne, may obtain further benefit from cyproterone acetate. This anti-acne medication contains a progestin with strong anti-androgen activity. Although not marketed as an OC, it has similar contraceptive efficacy. Another option may be the newer progestins such as desogestrel or norgestimate.⁷ These pills have been

Table 5

Dealing with Persistent BTB: Five Steps

1. Prepare patient at time of prescription that this may occur.
2. Look for and manage contributing factors such as poor compliance, chlamydia infection of the cervix, and cigarette smoking.
3. Provide reassurance and wait (rate of BTB decreases to about 10% at six months.)
4. Try a seven to ten day course of estrogen (*i.e.*, 1 mg 17 Beta-estradiol or 0.625 mg conjugated estrogen daily)
5. After three months, consider switching to a higher estrogen dose; a monophasic preparation; or a new generation progestin, although the evidence for this is not consistent.

demonstrated to reduce acne, although no direct comparisons with older progestins have proven them more effective.

Women taking anti-seizure medications may experience decreased efficacy due to increased hepatic metabolism of estrogen, the exceptions being valproic acid and gabapentin. In these women, a 50 µg ethinylestradiol formulation may be a better choice. Another alternative is to eliminate the 7-day pill-free interval in the low-dose pills, thereby decreasing follicular development.⁴

How to manage side effects

More important than initial selection is managing side effects, to keep patients from discontinuing the chosen OC. Nuisance side effects (Table 4) are the main reason for discontinuation rates up to 60%.^{5,8} There are three important principles to consider when managing these side effects: appropriate counselling at the time of prescription, clear instruction in the proper use of the OC, and reassurance as to the transient nature of most side effects.

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Nausea

Measures to manage nausea include taking the pill at night before sleep, or using an anti-nauseant such as dimenhydramine. If nausea persists after three months or more, it may help to switch to a lower dose (*i.e.*, 20 µg ethinyl estradiol) preparation.⁹

Breast tenderness

This will usually resolve within a few months of use. If breast tenderness persists, switching to a lower dose estrogen formulation may help.⁹

Headaches

In most women, headaches are a transient side effect. There is no support in the literature for using a lower dose estrogen, although this does make sense. If headaches are new and there are neurologic features, then the pill should be discontinued and a non-estrogen contraceptive method should be sought. Make sure that the headaches are not due to an estrogen withdrawal during the pill-free interval, in which case supplemental estrogen (*i.e.*, an estrogen patch) may be helpful.

Weight gain

Although OCs are widely perceived to cause weight gain, the literature shows no mean weight change in users of low dose OCs. Patient reassurance in this regard is important at the time of prescription. It may be helpful to record the patient's weight at the time of prescription, in order to either validate or refute subsequent claims of weight gain.

Mood/libido effects

These effects, presumed to be due to progestin, are difficult to study. There is no uniformly effective means of dealing with this side effect. Of note, the literature does not support any true increase in the rate of clinical depression with the use of OCs.

Break-through bleeding

BTB occurs in 25% of new OC users⁴, and is the primary reason for early pill discontinuation.⁸ (Refer to Table 5 for steps in dealing with persistent BTB.) In general, the first response of clinicians is to switch to another formulation, although there is no good rationale to guide these switches. It is difficult to make compar-

Shouldn't the first depression
be the last depression?



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isons between different products with regards to BTB.¹⁰ Studies in this area are limited by small sample size, poor controls for others factors that may affect bleeding, and variation in how BTB is defined and measured. There is no evidence that monophasic pills offer better cycle control than multiphasics, although there is some evidence that they may cause less endometrial atrophy, a contributing cause of BTB.⁷ Similarly, there is no solid evidence that cycle control varies with type of progestin.

Other factors that affect cycle control include poor compliance, chlamydia infection of the cervix, and cigarette smoking.¹⁰ Before switching formulations, these possibilities should be addressed.

Conclusion

The numerous OCs on the Canadian market are all considered safe and effective. For most users, no significant clinical differences exist between formulations, however certain individuals may benefit from particular formulations as suggested in this article.

Nuisance side effects can be managed with reassurance as to their transient nature, or managed with simple measures. Sometimes after appropriate waiting, a thoughtful switch of formulation is beneficial. [CME](#)

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For a quick-take on this article, go to our Frequently Asked Questions department on page 24.

Take-home message

- For most women, any low-dose pill (*i.e.*, 35 µg or less of ethinyl estradiol) is acceptable.
- The “mini-pill” does not reliably suppress ovulation, with 50% of users continuing to have regular ovulatory cycles.
- Managing side effects by appropriate counselling, clear instructions for proper use, and reassurance as to the transient nature of most side effects is essential. Nuisance side effects are the main reason for discontinuation rates of up to 60%.

Oral Contraceptives

As presented at Queen's University

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1. Which OC should I start my patients on?

No oral contraceptive (OC) has been demonstrated to be superior to another.

What pill to start depends upon personal opinion. I start patients on a low-dose preparation (30-35 µg of ethinyl estradiol). Theoretically, the new progestins (norgestimate and gestodene) have less effect on carbohydrate and lipid metabolism and, therefore, may be preferred. If a patient has done well previously on a particular low-dose oral contraceptive pill, I select that one. I use monophasic preparations in patients who have severe menstrual symptoms, as they are easier to administer continuously, or for sophisticated users who want to occasionally manipulate their cycles for convenience.

For an in-depth article on Oral Contraceptives, please go to page 63.

2. How do I decide which OC to switch to if my patient is bothered by side effects?

There is no consistent evidence to guide us when switching formulations to reduce side effects. Most importantly, be patient and reassure the patient that most nuisance side effects are transient. If they persist, a lower-dose formula may be helpful. See page 63 for additional tips.

3. What if my patient is unable to tolerate OCs?

There are other effective methods of birth control besides the oral contraceptive pill. Patients may prefer the convenience and side effect profiles of the copper intrauterine device, the progestin intrauterine contraceptive system (Mirena™), or Depo-Provera™. These products are good alternatives to the OCs, especially in certain patients.