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Recycling the Cycle – Extended and Continuous Use of Combined Hormonal Contraceptives

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Statement of objectives

Upon completion of this lesson, the pharmacy technician will be able to:

1. Describe the different combined hormonal contraceptive regimens that women may be following including a standard regimen, an extended regimen and a continuous regimen.
2. Understand the advantages and disadvantages of extended or continuous combined hormonal contraceptive regimens.
3. Understand the rationale for choosing one combined hormonal contraceptive product or regimen over another.
4. Recognize situations where a patient taking a combined hormonal contraceptive may benefit from a consultation with the pharmacist.

Introduction

Combined oral contraceptives (COCs) have been available on the Canadian market since the 1960s and continue to provide a safe and effective method of reversible contraception for women across the reproductive age span. Over the years, hormone doses have been reduced in order to improve safety and tolerability of these products while maintaining contraceptive effectiveness. The development of the combined hormonal contraceptive (CHC) patch and the CHC vaginal ring provide women with alternatives to the traditional oral dosage forms and may aid patient compliance. Recently, extended and continuous CHC regimens have become more popular. Pharmacists and technicians working in community practice frequently encounter women of childbearing age, so it is essential for them to be familiar with all aspects of CHCs, including the potential advantages and disadvantages of these newer regimens.

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CHC components and characteristics

CHCs contain the synthetic estrogen, ethinyl estradiol (EE), and one of various synthetic progestins. Products containing 35 µg of EE or less per daily dose are considered low-dose preparations.[1, 2] Estrogen contributes to the contraceptive effect by suppressing ovulation and also helps to stabilize the endometrium to prevent irregular or unscheduled uterine bleeding.[3] The progestin component of the CHC is primarily responsible for the contraceptive effect by suppressing ovulation, thickening cervical mucus and making the endometrial lining unreceptive to a fertilized ovum.[3] CHC progestin doses are adjusted to account for their varying potencies; therefore, all available products are effective as contraceptives.[3]

Adverse effects, safety and non-contraceptive benefits

Most women tolerate CHCs well. For the majority of patients, any adverse effects usually resolve within the first few months of use.[2] It is important for patients to be aware of this. Of women who stop taking their CHCs because of side effects, most do so within the first two months of use.[4] Discontinuation may put patients at risk of pregnancy.

The most common adverse effects of CHCs are headaches, nausea and breast tenderness and these occur with similar frequency with all CHCs.[5] Some women may experience mood changes with CHCs.[6] Weight gain is often a concern, but based on reviews of available evidence, no large effect is evident.[7] Unexpected bleeding is estimated to occur in 10-30% of CHC users in the first three months of use.[1] Breakthrough bleeding (BTB) and spotting (very light bleeding) are not harmful and do not necessarily indicate a lack of contraceptive efficacy; however, women may see this as an unacceptable nuisance. It is important for women to have a consistent daily pill-taking time because late or missed doses are a common cause of BTB.[8] Again, this adverse effect usually resolves with continued use. Frequent product changes to attempt to resolve this problem are not recommended.[9]

Cardiovascular risks associated with CHCs are minimal in most healthy, non-smoking women. The risk of blood clots increases slightly and is generally higher in the first year of use.[10, 11] Low-dose CHCs are not associated with an increased risk of myocardial infarction or stroke.[12] It is unknown how older age or the presence of other cardiovascular risk factors, such as diabetes, further impact these risks. Evidence is conflicting regarding the effect of CHCs on breast cancer risk; risk may increase slightly or not at all with current use.[13, 14]

CHCs provide many non-contraceptive benefits and may be used solely for this purpose. Many women rely on CHCs for cycle control or regulation of irregular, heavy or painful periods. Cycle control refers to the ability of a CHC to produce uterine bleeding that is minimal and occurs at predictable times in the cycle. CHCs reduce menstrual cramps and pain and can decrease menstrual flow (the number of bleeding days and amount of blood loss) by 60%.[15] The use of CHCs is associated with protection against ovarian and endometrial cancers, and possibly a reduced risk of colorectal cancer, and these effects may persist for many years after discontinuing CHCs.[16] Other non-contraceptive benefits of CHCs include decreased acne and facial hair growth, increased bone mineral density, decreased perimenopausal symptoms, decreased risk of fibroids and decreased pelvic inflammatory disease.[1,15,17]

New CHC regimens

When COCs were first developed, the standard 21/7 regimen was designed to mimic a regular 28-day menstrual cycle. This was seen as natural by women, their physicians and the Catholic Church.[18] At the time, no consideration was given to alternate regimens. With the 21/7 regimen, women take hormones for 21 days followed by a 7-day hormone-free interval (HFI) during which menstrual bleeding occurs. The cycle is then repeated. The bleeding that occurs with this regimen is not biological, but is induced by the drop in hormone levels that occurs when hormone-containing tablets are stopped.

The idea of altering the standard CHC regimen is not new, but has certainly gained popularity in recent years. With an extended regimen, women take hormones for more than 21 days, resulting in longer intervals between episodes of withdrawal menstrual bleeding. The HFI may also be shortened to less than seven days or eliminated completely. For example, women may take hormones cyclically for 24 days followed by a 4-day HFI. With a continuous regimen, women take hormones without interruption and menstrual bleeding can be prevented or suppressed. Most importantly, hormones should never be taken for fewer than 21 consecutive days and the HFI should never be longer than 7 days.

An extended use CHC recently became available on the Canadian market. The product provides 84 days of hormone containing tablets followed by seven inactive tablets. Women who take this will experience only four menstrual periods per year. All currently available CHC products that provide 35 µg EE per day or less, including the patch and vaginal ring, can be used on an extended or continuous basis.[18] Both monophasic and multiphasic products may be taken in this way. Until long-term studies are conducted with extended or continuous CHCs, adverse effects, safety and non-contraceptive benefits are assumed to be similar to those of standard cyclic CHCs as discussed in the sections above.[18]

Table 1

Most common adverse effects of CHCs

- headaches
- nausea
- breast tenderness
- mood changes
- weight gain
- breakthrough bleeding (BTB) or spotting

Advantages of extended or continuous use of CHCs

Using CHCs on an extended or continuous basis may improve contraceptive efficacy. During the seven day HFI of a standard 21/7 regimen, an ovarian follicle may start to develop.[19] If the HFI is inadvertently lengthened by missing pills at the

end of one cycle or near the beginning of another, or if a woman forgets to re-start her CHC after the HFI, ovulation and pregnancy could occur. Shortening or eliminating the HFI may decrease the chance of this happening.

Cycle-related symptoms are those that start before and continue during menstrual bleeding. Women may experience symptoms including breast tenderness, bloating, abdominal discomfort and headaches or migraines during the HFI of standard 21/7 CHC regimens.[20] These symptoms are likely related to fluctuating levels of hormones. For example, migraine headaches can be triggered by estrogen withdrawal which occurs prior to the start of a menstrual period. [21] Extending the duration of hormone-containing tablets beyond 21 days can eliminate cycle-related symptoms by maintaining relatively constant hormone levels for a prolonged length of time.[22]

Suppressing or delaying menstrual periods with extended or continuous CHC use may be beneficial for certain other patients. Women with endometriosis may experience reduced frequency and intensity of menstrual pain, pain during intercourse and non-menstrual pelvic pain. [18] Perimenopause is the period of time prior to menopause when fluctuating hormone levels can contribute to irregular menstrual cycles and symptoms including hot flashes, night sweats and sleep disturbances. With cyclic use of CHCs, perimenopausal symptoms may return during the 7-day HFI; however, extended or continuous use may be helpful for ongoing symptom control.[18]

Other potential benefits of an extended or continuous CHC regimen are cost savings and increased productivity. Fewer menstrual periods may result in reduced need to purchase sanitary products. Women on continuous regimens may stop having periods altogether. This savings must be balanced against the need to purchase eighteen 21-day pill packages per year to take a CHC continuously versus thirteen pill packages per year to take a CHC cyclically. It is also likely that women with severe cycle-related complaints will miss fewer school or work days when symptoms occur with reduced frequency or are eliminated completely.

Disadvantages of extended or continuous use of CHCs

With a standard 21/7 regimen, withdrawal menstrual bleeding occurs at predictable times, usually starting within a few days of taking the last active tablet in the pill package. With an extended regimen, bleeding may occur at less frequent, but predictable intervals. Ideally, with a continuous regimen, menstrual bleeding should be completely suppressed resulting in amenorrhea or no menstrual periods. The main downside to extended or continuous use of CHCs is the occurrence of irregular and unpredictable breakthrough bleeding or spotting. The incidence is similar to that seen with cyclic use and usually decreases with time. Over time, an extended or continuous CHC regimen will result in fewer total bleeding days compared to a standard 21/7 regimen.[18]

Choice of CHC

The best CHC for a patient is the one that provides effective contraception and acceptable cycle control with minimal adverse effects.[1] It is preferable to use a product with the lowest effective dose of estrogen, so starting with the lowest available dose is reasonable.[1, 2]

The choice of dosage form may depend on patient preference or experience. The CHC patch or vaginal ring may be preferred for patients who get nauseated or frequently miss doses of COCs.

The choice of regimen may also be based on patient preference. Some women may prefer the standard 21/7 regimen because they feel that monthly withdrawal bleeding is natural and provides reassurance that they aren't pregnant. Others may be happy to have less frequent periods and opt for an extended or continuous regimen. The physician will often recommend a particular regimen based on the patient's history of cycle-related symptoms, medical conditions or adverse effects exacerbated by a different regimen.

The technician's role

It is important for technicians to be aware of the different CHC products available and the different regimens that patients may be following. When a patient presents to the pharmacy with a CHC prescription with directions written as "Take as directed," clarifying the regimen as standard 21/7, extended or continuous will ensure that the patient receives the correct amount of medication over a given period of time. Knowing how a CHC is taken is necessary for monitoring compliance. Technicians can evaluate a patient's consistency of CHC use when filling refills.

Healthcare providers should be the focal point of efforts to help women become more successful CHC users because they can have a positive impact on adherence, continuance and patient satisfaction.[23] Patients frequently encounter pharmacy technicians when they call or approach the pharmacy with their concerns; therefore, it is essential for technicians to recognize when referral to the pharmacist is necessary. The following situations are examples of when patients may benefit from a pharmacist consultation:

- a patient is receiving her first CHC;
- a patient is receiving a new CHC dosage form (eg. patch or ring);
- a patient says that she thinks her CHC is making her gain weight;
- a patient asks whether her CHC will increase her risk of breast cancer;
- a patient is buying a natural health product and asks if it will interact with her CHC;
- a patient receives a prescription for an antibiotic; the pharmacy's computer system detects a drug interaction between the antibiotic and the patient's CHC;
- a patient calls the pharmacy and says that she has just forgotten to take her last two birth control pills;
- upon reviewing a patient's profile, it is apparent that a patient's CHC is not being refilled on a regular basis;
- a CHC patient says that she has had unprotected intercourse and thinks she may need to use emergency contraception.

There may be other instances when pharmacist referral is necessary. When a patient is picking up a CHC refill, this is a good opportunity for the technician to ask the patient if they have any questions or concerns for the pharmacist. Technicians should also be sensitive to the discomfort that women may feel when discussing sexuality and contraception. Patients may be directed to semi-private or private counseling areas if necessary.

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➤ QUESTIONS

Please select the best answer for each question or answer online at www.pharmacygateway.ca for instant results.

1. Examples of possible combined hormonal contraceptive (CHC) regimens include all of the following EXCEPT:
a) Taking hormones for 24 days followed by a 7-day HFI
b) Taking hormones for 24 days followed by a 4-day HFI
c) Taking hormones for 84 days followed by a 7-day HFI
d) Taking hormones for 20 days followed by a 4-day HFI

2. With regards to the contraceptive effect of CHCs, which of the following statements is TRUE?
a) Estrogen alone is responsible for the contraceptive effect.
b) Progestin alone is responsible for the contraceptive effect.
c) Both estrogen and progestin contribute to the contraceptive effect.
d) Contraceptive effect is not as good with low-dose CHC formulations.

3. With regards to extended or continuous use of CHCs, which of the following statements is FALSE?
a)Any currently available combined hormonal contraceptive (CHC) can be taken on an extended or continuous basis.
b) Multiphasic products should not be used on a continuous basis because hormone fluctuations will result in adverse effects.
c) If a woman wanted to use the CHC patch continuously, she would apply and change one patch every week.
d) If a woman wanted to use the CHC vaginal ring continuously, she would remove and insert one ring every 21 days.

4. Cardiovascular risks associated with the use of low-dose extended or continuous CHCs in healthy, non-smoking women include which of the following:
a) Increased risk of heart attacks
b) Increased risk of strokes
c) Increased risk of blood clots
d) All of the above
e) None of the above

5. Non-contraceptive benefits of extended or continuous CHCs include all of the following EXCEPT:
a) Reduced menstrual blood loss
b) Reduced risk of endometrial and cervical cancer
c) Improved symptoms of perimenopause
d) Improvements in acne and reduced growth of facial hair

6. Breakthrough bleeding (BTB) and spotting are common occurrences in CHC users. Which statement is FALSE?
a) BTB is an indication that the CHC dose is incorrect and the product should be changed.
b) Inconsistent pill-taking can contribute to BTB and spotting.
c) BTB usually resolves after the first few months of CHC use.
d) BTB may occur with a standard 21/7 regimen or with a continuous regimen.

7. Which of the following statements about the hormone-free interval (HFI) is TRUE?
a) During the 7-day HFI of a standard 21/7 regimen, development of an ovarian follicle is suppressed.
b) Missing pills prior to a 7-day HFI may reduce the possibility of ovulation occurring in the next cycle.
c) The HFI will be lengthened if a woman forgets to start her next pill package.
d) Shortening or eliminating the HFI may increase the chance that ovulation could occur.

8. What are the disadvantages of extended use of CHCs?
a) Breakthrough bleeding occurs more frequently than with a standard 21/7 regimen.

b) Cycle-related symptoms are more severe when they occur, even though they are less frequent.
c) Breakthrough bleeding and spotting may occur at irregular and unpredictable times.
d) All of the above

9. With regards to adverse effects of CHCs, which of the following statements is FALSE?

a) Most adverse effects will resolve within the first few months of use.
b) The most common adverse effects of COCs are headaches, nausea and breast soreness.
c) Weight gain is a common adverse effect of CHCs.
d) Stopping a CHC because of adverse effects may increase the chance of pregnancy.

10. Which of the following situations DOES NOT necessitate referral to the pharmacist?

a) A patient calls the pharmacy wondering what she should do because she has just missed taking two days of her CHC.
b) A patient who is taking a CHC on a continuous basis comes into the pharmacy to pick up a refill of her CHC and expresses frustration that she is having frequent breakthrough bleeding.
c) A patient is picking up her first prescription for a CHC.
d) A patient is picking up her second prescription for a CHC and reports that she has no questions or concerns about it.

11. Cycle-related symptoms include all of the following EXCEPT:

a) Breakthrough bleeding
b) Headaches or migraines
c) Abdominal cramps and bloating
d) Sore breasts

12. Possible advantages of continuous use of CHCs include all of the following EXCEPT:

a) Enhanced pregnancy prevention because of reduced chance of ovulation
b) Decreased costs related to purchasing sanitary supplies because of menstrual suppression
c) Decreased frequency of pain due to endometriosis
d) Fewer adverse effects of CHCs such as headaches and weight gain

13. Which factors are usually taken into consideration when a CHC product and regimen are chosen for a patient?

a) Patient preference for a tablet, patch or ring
b) Patient preference for frequency of withdrawal menstrual bleeding
c) Estrogen dose required for effective pregnancy prevention
d) All of the above

14. Which of the following patients might NOT prefer an extended or continuous CHC regimen?

a) A female military recruit on active duty
b) A female athlete who experiences severe cramping and headaches with her period each month
c) A woman who feels that monthly periods are normal, healthy and natural
d) All of the above

15. A patient presents you with a prescription for a COC as a 21-day package and written to "Take as directed" for one year. What should you do in this situation?

a) Ask the patient whether she is following a standard 21/7, extended or continuous regimen and fill the prescription accordingly.
b) Since the standard 21/7 regimen is most common, assume that this is what the physician intends and fill the prescription for 13 packages.
c) Assume that the physician intends for the patient to take the COC continuously and fill the prescription for 18 packages.
d) Suggest that the patient return to her physician to get a new prescription with specific directions.

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