CHIPS REGIMEN

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THE SUCCESS STORY CONTINUOUS CONTRACEPTIVE PILLS

Combined oral contraceptive pills (OCP) act by inhibiting ovulation at the level of the pituitary and hypothalamus, via suppression of gonadotropin secretion. The estrogen component prevents the increase in follicle-stimulating hormone (FSH), thus inhibiting the formation of a dominant follicle. The progestin molecule inhibits luteinizing hormone (LH) secretion and thus keeps the LH surge from occurring. Both together prevent the occurrence of ovulation.

Progesterone is not normally present at significant levels in the non-luteal phase of the normal menstrual cycle. During the luteal phase, the endometrium has already become thickened and it is now decidualized by the action of progesterone. With a combined OCP, the progesterone shows stronger activity than the estrogen, causing the endometrium to become thin but decidualized.

The endometrial glands show atrophy, and the uterus is not receptive to implantation if fertilization occurs. Additional contraceptive effects are caused by the change in cervical mucus characteristics to become thick and impermeable. This keeps sperm from swimming up to reach the uterine cavity and then the fallopian tubes, where fertilization occurs.

Moreover, the tubal motility decreases, hindering sperm and ovum movement through the fallopian tube and thus preventing efficient fertilization.

With progestin-only pills, effective contraception is possible, but the addition of estrogen adds to its efficacy by preventing follicular development, stabilizing the endometrium and perhaps preventing breakthrough bleeding, which is more common with the former. Estrogen also up-regulates estrogen receptors within the cells, allowing for the dose of progesterone to be reduced.

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Extended and continuous-use pills

Traditional oral contraceptive pills are designed to deliver a low dose of female sex hormones, either estrogen and progesterone in combination, or progesterone alone, for 21 days, with a fourth week without any hormones. This leaves time for endometrial shedding, called withdrawal bleeding. However, this phenomenon is quite different from menstrual bleeding and is not really essential for a woman's health. For this reason, many scientists in the field of reproductive health have been examining the feasibility and safety of using birth control pills continuously, without monthly withdrawal bleeds.

There are two ways in which this can be done. One is called continuous-use birth control and the other is extended-use birth control. In the first type, the hormone pills are taken without a break for a year or more, which means there are no withdrawal bleeds. In the second case, the active pills are taken for more than 21 days, thus reducing the number of withdrawal bleeds experienced over a year, but not stopping them altogether.

Almost any combined estrogen-progestin oral contraceptive can be used in either of these ways. However, some formulations are available that are specifically designed to provide a longer gap between periods, with active pills being taken for 84 days (12 weeks) or one year, respectively.

Mechanisms of action of extended- or continuous-use pills

With the typical 28-day pill cycle, active hormones are taken for 21 days, during which time progesterone action is observed on the endometrium. During the next 7 days, the placebo allows unopposed estrogen action. Since there is no FSH inhibition, estradiol is produced by the ovaries. This leads to endometrial growth which is promptly suppressed by the active pills. The aim of continuous- or extended-use

is thus to eliminate the growth of the endometrium, thus preventing withdrawal bleeding. Breakthrough bleeding occurs due to endometrial atrophy and not endometrial shedding, as there is no thickened decidualized endometrium to shed.

What are the benefits?

- Continuous- or extended-use OCPs are highly effective in preventing pregnancy.
- This risk is reduced since there is no break in active pill use, and hence a lower chance of missing the start date for active pills. No significant difference is seen with contraceptive efficacy in cyclic vs extended- or continuous-use OCP.
- Conditions that are aggravated by menstruation such as endometriosis or anemia may also be benefited from this treatment, as also premenstrual bloating, mood swings, premenstrual tension, headaches, or breast tenderness. Some women develop migraine and other headaches in the week off active pills, which can be avoided by continuing them without a break.

What are the risks?

Delaying periods for a long time can cause a higher rate of breakthrough bleeding or spotting – bleeding between periods – that can be inconvenient or embarrassing. This is more often experienced in the first few months of continuous use. As the physiology adapts to the low-dose continuous regimen, such phenomena typically decrease over time.

Conclusions

Continuous use of OCPs is both safe and reliable as a method of contraception, with the hormonal and metabolic effects being similar to cyclic use. Reduced period frequency is desirable for women with dysmenorrhea and menstruation-related symptoms, with good patient satisfaction.

There are no additional contraindications to the use of continuous OCPs than those in force for cyclic OCP use, and endometrial changes are beneficial with the former compared to the latter.

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DIFFERENCES IN SIDE EFFECTS BUT EQUAL BENEFITS PROVIDED BY TWO TYPES OF BLOOD PRESSURE DRUGS

People who are just beginning treatment for high blood pressure can benefit equally from two different classes of medicine - angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) - yet ARBs may be less likely to cause medication side effects. While the class of blood pressure-lowering medicines called angiotensin-converting enzyme (ACE) inhibitors may be prescribed more commonly, angiotensin receptor blockers (ARBs) work just as well and may cause fewer side effects. Currently, ACE inhibitors are prescribed more commonly than ARBs as a first-time blood pressure control medicine.

Both types of medicines work on the renin-angiotensin-aldosterone system, a group of related hormones that act together to regulate blood pressure. ACE inhibitors lower blood pressure by blocking an enzyme early in the system so that less angiotensin, a chemical that narrows blood vessels, is produced, and blood vessels can remain wider and more relaxed. ARBs block receptors in the blood vessels that angiotensin attaches to, diminishing its vessel-constricting effect.

In professional guidelines, several classes of medications are equally recommended as first-line therapies. With so many medicines to choose from, we felt we could help provide some clarity and guidance to patients and health care professionals.

The AHA/ACC 2017 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults says the primary medications for treating high blood pressure are thiazide diuretics, ACE inhibitors, ARBs, and calcium channel blockers as they have been shown to reduce cardiovascular events. Physical activity and other lifestyle changes are recommended for managing all levels of high blood pressure, even if medication is required.

Health records for patients who began first-time blood pressure-lowering treatment with a single medicine between 1996 and 2018 were reviewed for this study. Researchers compared the occurrence of heart-related events and stroke among 2,297,881 patients treated with ACE inhibitors to those of 673,938 patients treated with ARBs. Heart-related events include heart attack, heart failure or stroke, or a combination of any of these events or sudden cardiac death recorded in the database. The researchers also compared the occurrence of 51 different side effects between the two groups. Follow-up times varied in the database records, but they ranged from about 4 months to more than 18 months.

They found no significant differences in the occurrence of heart attack, stroke, hospitalization for heart failure, or any cardiac event. However, they found significant differences in the occurrence of four medication side effects. Compared with those taking ARBs, people taking ACE inhibitors were: • 3.3 times more likely to develop fluid accumulation and swelling of the deeper layers of the skin and mucous membranes (angioedema); • 32% more likely to develop a cough (which may be dry, persistent, and bothersome); 32% more likely to develop sudden inflammation of the pancreas (pancreatitis); and

• 18% more likely to develop bleeding in the gastrointestinal tract; Nodifference were detected in two types of medicine in reducing the complications of hypertension, but we did see a difference in side effects. If a patient is starting hypertension therapy for the first time, our results point to starting with the ARB over the ACE inhibitor."

ARBs do not differ in effectiveness and may have fewer side effects than ACE inhibitors among those just beginning treatment. We unfortunately cannot extend these conclusions to people who are already taking ACE inhibitors or those who are taking multiple medications.

The study is limited by wide variation in the length of time patients were included in the different databases. Although many people were followed for a long period of time, those who had shorter follow-up periods may not have taken the medications long enough to experience their full benefits in preventing cardiovascular disease events. Most of the participants taking ACE inhibitors (80%) were taking lisinopril, and the most used ARB (45% of those taking this class of medication) was losartan, so the results may not be fully generalizable to other medicines in these classes. It is also important to note that results from this analysis of first-line therapy may not be generalizable to people with hypertension who have been prescribed combination treatment or who switch from one type of medication to another.

In addition to encouraging patients to live a healthy lifestyle and taking medication as prescribed to control blood pressure, the American Heart Association recommends regular self-blood pressure monitoring with a validated device and working with a health care professional on a plan to reduce blood pressure.

JANUS KINASE (JAK) INHIBITORS : DRUGSAFETY COMMUNICATION FDA REQUIRES WARNINGS ABOUT INCREASED RISK OF SERIOUS HEART- RELATED EVENTS, CANCER, BLOOD CLOTS, AND DEATH

The FDA is requiring revisions to the Boxed Warning, FDA's most prominent warning, for Xeljanz/Xeljanz XR (tofacitinib), Olumiant (baricitinib) and Rinvoq (upadacitinib) to include information about the risks of serious heart-related events, cancer, blood clots, and death.

Based on the review of a large randomized safety clinical trial, the FDA has concluded there is an increased risk of serious heart-related events such as heart attack or stroke, cancer, blood clots, and death with the arthritis and ulcerative colitis medicines Xeljanz and Xeljanz XR. This trial compared Xeljanz with another type of medicine used to treat arthritis called tumor necrosis factor (TNF) blockers in patients with rheumatoid arthritis. The trial's final results also showed an increased risk of blood clots and death with the lower dose of Xeljanz.

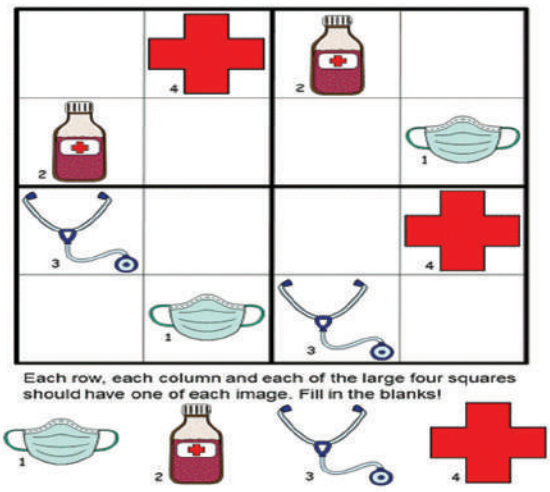
The FDA is requiring new and updated warnings for two other arthritis medicines in the same drug class as Xeljanz, called Janus kinase (JAK) inhibitors, Olumiant and Rinvoq. Olumiant and Rinvoq have not been studied in trials similar to the large safety clinical trial with Xeljanz, so the risks have not been adequately evaluated. However, since they share mechanisms of action with Xeljanz, FDA considers that these medicines may have similar risks as seen in the Xeljanz safety trial.

Background: Xeljanz/Xeljanz XR, Olumiant, and Rinvoq are used to treat certain serious, chronic, and progressive inflammatory conditions. All three medicines are approved to be used alone or with other drugs to treat rheumatoid arthritis, a condition in which the body attacks its own joints, causing pain, swelling, joint damage, and loss of function. Xeljanz is also approved to treat psoriatic arthritis, a condition that causes joint pain and swelling; ulcerative colitis, which is a chronic, inflammatory disease affecting the colon; and polyarticular course juvenile idiopathic arthritis, a type of childhood arthritis.

Recommendations: Patients who are taking Xeljanz/Xeljanz XR, Olumiant, or Rinvoq should tell their health care professional if they are a current or past smoker, or have had a heart attack, other heart problems, stroke, or blood clots in the past as these may put them at higher risk for serious problems with the medicines. Patients starting these medicines should also tell their health care professional about these risk factors. Patients should seek emergency help right away if they have any symptoms that may signal a heart attack, stroke, or blood clot. Treatment with these medicines is associated with an increased risk of certain cancers including lymphoma and lung cancer. Patients should also talk to their health care professional if they have any questions or concerns.

Health Professionals should consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Xeljanz/Xeljanz XR, Olumiant, or Rinvoq. This is particularly the case in patients who are current or past smokers, those with other cardiovascular risk factors, those who develop a malignancy, and those with a known malignancy other than a successfully treated nonmelanoma skin cancer. Reserve these medicines for patients who have had an inadequate response or intolerance to one or more TNF blockers. Counsel patients about the benefits and risks of these medicines and advise them to seek emergency medical attention if they experience signs and symptoms of a heart attack, stroke, or blood clot.

Health Care Sudoku



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