



## Professional article

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Niš, Serbia**CONTRACEPTION FOR WOMEN  
WITH MEDICAL DISORDERS****SUMMARY**

**This paper describes some of the issues which should be considered when advising women with certain chronic medical conditions in making appropriate contraceptive choice. Women should not be unnecessarily restricted and should be enabled to make informed decisions about their choice of contraception. The effect of contraception on the medical condition and the effect of the condition on contraceptive use should be considered. The possibility of drug interactions or secondary conditions associated with the chronic condition may influence contraceptive choice.**

**Key words: contraception, medical disorders**

**INTRODUCTION**

In women with certain medical disorders, both pregnancy and contraception can present extra hazards. Individual contraceptive choice must be balanced against the risk of unintended pregnancy and should not be unnecessarily restricted by underlying medical conditions. Clinicians should consider: the effects of contraceptive use on the medical condition, the effects of the condition on contraceptive use, potential drug interactions and concurrent medical conditions. The method chosen should provide effective and safe contraception which poses minimal health risk. The potential health benefits of various contraceptives need to be considered (1,2). Knowledge and empathic counseling can help a woman cope with her illness; ignorance or misinformation can be life-threatening. The supportive role of the partner in choice and use of the method is particularly important. The World Health Organization (WHO) medical eligibility criteria for contraceptive use provides helpful guidance on the safe use of contraception (3,4). The following ones are some common medical disorders

that require special attention from those offering contraceptive advice. Methods not mentioned in relation to a particular medical disorder can be used without restriction.

**CARDIOVASCULAR DISEASES**

Cardiovascular diseases with special implications for contraception include: venous thromboembolism, ischemic or valvular heart disease, and hypertension. For these women pregnancy may also pose additional risks, and, therefore, effective contraception may be of special importance.

*Venous thromboembolism*

Venous thromboembolism (VTE) essentially encompasses: deep vein thrombosis of the legs, pulmonary embolism and cerebral sinus thrombosis. It results from a combination of inherited and acquired risk factors. Inherited thrombophilias are: antithrombin, protein C, protein S or factor XII deficiency, activated protein C resistance (Factor V

Leiden mutation) etc. A feature which is common to thrombophilic families is that the age of first thrombosis manifestation is much younger than for consecutive patients with thrombosis, irrespective of the underlying defect and even when no defect has been identified (5,6). Acquired risk factors are: immobility, trauma, surgery, obesity, pregnancy/ puerperium, long distance travel, antiphospholipid antibody lupus anticoagulant, use of combined oral contraception (COC) or hormone replacement therapy (5,7).

Women with known hereditary thrombophilias are at high risk of deep vein thrombosis in pregnancy, and the use of effective contraception in these women is imperative (2,4). Factor V Leiden mutation (an autosomal dominant pattern) is the most common genetic cause of primary and recurrent VTE in the pregnant and non-pregnant women and it accounts for approximately 20% -50% of pregnancy-related venous thrombosis cases. This mutation shifts the coagulation system toward hypercoagulability. A synergistic effect has been shown for Factor V Leiden mutation and COC use. The risk of VTE for women who use COCs is 30, and for Factor V Leiden mutation carriers 57 per 100.000 woman per year. However, for women who are carriers and who use COCs, the risk amounts to 285 per 100.000 per year (5). Screening all women who wish to use COC for thrombophilias is pointless (it is not cost-effective). A major problem with screening is that currently, even in individuals who have had a VTE, a coagulation defect can only be detected in about 50%. This means that a negative screen does not give complete reassurance; bearing this in mind, if a woman wishes to take COC, it can be prescribed. It should be also borne in mind that the greatest risk of VTE occurs in the first year of pill use. Thus, if a woman has already been on the pills for over a year without having developed VTE, she is likely to be at reduced risk (5,8,9). Recommended criteria for factor V Leiden screening: any thrombosis at age <50, venous thrombosis at unusual sites (hepatic, mesenteric, cerebral veins), venous thrombosis in pregnant women or women using oral contraceptives, recurrent venous thrombosis, relatives of individuals who develop venous thrombosis under the age of 50, myocardial infarction in female smokers under the age of 50. Testing may be considered: women with recurrent pregnancy loss or unexplained severe preeclampsia, placental abruption, intrauterine fetal growth retardation or stillbirth, relatives of individuals known to have factor V Leiden or venous thrombosis at the age > 50, except when active malignancy is present (9).

Since VTE is a multifactorial problem, even women without a family history may have risk

factors which make taking the COCs inadvisable. Body mass index (BMI) above 30 kg/m<sup>2</sup> and smoking have recently emerged as significant risk factors for VTE in COC users: BMI >25 kg/m<sup>2</sup> carries up to a six-fold risk of VTE, while smoking doubles the risk. Recent data suggest no difference in VTE rates between second and third generation pills (5).

For women with history of VTE, the use of COC is contraindicated because synthetic estrogens increase the risk of deep venous thrombosis (2,4).

It is often assumed that women with varicose veins should be cautious about taking the pill, but this is not substantial. However, women should be reminded to stop taking the pill about 4 weeks prior to major surgery or immobility and not to resume for the same length of time afterwards (5).

Progestogen only methods are suitable for women at risk of VTE: progestogen only pills, injectables, implants and levonorgestrel-releasing intrauterine system (Lng-IUS, Mirena) (5). Even though there have not been published studies on the use of the Lng-IUS in women with thrombophilia, a history of VTE or thrombophilia have become conditions in which the use of progestogen only contraception including the Lng-IUS may be appropriate (2). Depot medroxyprogesterone acetate (DMPA) has a particular advantage in women with sickle cell disease (with its higher risk of thrombosis) as it has been shown to reduce the number of crises and improve the hematological picture (5).

Progestogen-only emergency contraception is also safe for use in these women.

Non-hormonal methods are theoretically suitable although barrier and natural family planning methods may have unacceptably high failure rates (5).

For women with any cardiovascular disease, the copper intrauterine contraceptive device (Cu-IUD) can be a good choice because its dose not have systemic effects and is highly effective with failure rates of less than 1 per 100 woman per year (4,5).

#### *Arterial diseases*

Combined oral contraception should not be used in women who have one major or multiple minor risk factors for arterial disease. It should be remembered that all risk factors (including age) interact. Major risk factors are: history of VTE, family history of VTE disease in first degree relatives aged <45, major surgery with prolonged immobilization, long-term immobility, sickle cell disease, smokers aged >35 years, hypertension >140/90 mmHg, past or present circulatory disease, family history of arterial disease in first degree relatives aged < 45, valvular heart disease, history of ischemic stroke, vascular disease, hyperlipidemia, migraine

with aura (10). Minor risk factors are: major surgery without prolonged immobilization, BMI>30, age >40, smokers aged <35, history of hemorrhagic stroke, migraine without aura (10,11).

Most important risk factors for arterial disease are: arterial hypertension, smoking and diabetes mellitus.

*Hypertension* on its own is a significant risk factor both for myocardial infarction and stroke. Women with mild hypertension (140-159/90-99 mmHg) and no other risk factors (smoking, diabetes, obesity or age over 35) may use low-dose COCs with careful monitoring when other contraceptive options are not available or acceptable to them. Moderate (160-179/100-109 mmHg) and severe (>180/110 mmHg) hypertension and hypertension complicated with vascular disease are contraindications for the use of COCs (3,4,12).

*Smoking* on its own increases the risk, and there is a multiplicative effect with the combined contraceptive pills. Smokers over 35 should not use estrogen-containing contraceptives (3,4,12).

For *diabetic women*, the most important medical factor which affects their choice of contraception is the presence of vascular complications. Since the incidence of vascular complications increases with age, women with diabetes should plan to have their children as early as possible. As pregnancy in diabetic women should be planned to occur when glucose control is optimal, the use of effective contraception is crucial. Women who had diabetes for less than 20 years or who have no vascular damage may use any hormonal contraception. They are largely unrestricted in their contraceptive choice, and low-dose COCs are widely used (3,4,12). There is no evidence to suggest that hormonal contraceptives antagonize the hypoglycemic effect of insulin and other antidiabetic drugs (1). Women who had diabetes for more than 20 years or who have diabetic vascular complications (including nephropathy, retinopathy or neuropathy) have more restrictive options. Use of COCs poses unacceptable health risk and should not be prescribed. Progestogen only injectables may also be considered but only if other methods are not available or acceptable to the client (3,4). Women may be advised that benefits of using the progestogen-only pills or implant or Lng-IUS may outweigh any risks (1). In addition, the use of the Lng-IUS reduces uterine bleeding, resulting in improved body iron stores (2). For parous diabetic women seeking contraception, or for women with complicated diabetes, non-hormonal contraception such as the Cu-IUD may be a good choice. However, these women are susceptible to infection and to avoid introduction of pathogens into the uterus, particular

attention should be given to good screening, treatment of pre-existing infection and maintenance of strict asepsis. Prophylactic antibiotics should be considered.

Women who already have significant arterial disease such as: *angina, ischemic heart disease, pulmonary hypertension* and *consistently raised blood pressure (over 160/95 mmHg)* cannot use estrogen containing contraception. Estrogen should also be avoided in *any arterial condition which predisposes to thrombosis*. However, such a condition does not apply to those with minor asymptomatic valvular abnormalities (5).

*The risk of myocardial infarction in women taking COCs* seems to increase only in association with other risk factors for arterial disease (7).

*The risk of ischemic stroke* is increased in COC users (5 per 100.000 woman per year) and is increased further in women who smoke or who are hypertensive, but it returns to normal after stopping the pills. In women who are under the age of 35 and who are normotensive non-smokers, the use of COCs does not increase the risk of hemorrhagic stroke. However, the pills double the risk in the over 35 age group. Again, smokers and hypertensive women are at increased risk (10,11).

The use of estrogen-containing contraceptives is contraindicated for women with a history of ischemic heart disease or stroke. These women and women with severe hypertension or hypertension with vascular disease can generally use progestogen-only contraception when other options are not available or acceptable (pills or implants but injectables only as the last choice) (4). Injectables tend to low high-density lipoprotein cholesterol which may make them less suitable than the low-dose methods. Caution is advisable in view of the severity of these conditions and the relative paucity of evidence (5).

Intrauterine contraception (Cu-IUD, Lng-IUS) is safe for use in women with a significant arterial disease but may require antibiotic cover at insertion and removal if there is any risk of bacterial endocarditis (1,4). Women on anticoagulants should be monitored particularly closely if using a Cu-IUD, since they are at greater risk of heavy bleeding. The Lng-IUS may be a suitable choice in these women (4).

Barrier methods and natural methods are not effective enough when the risk associated with pregnancy is so great (5). Women with severe arterial disease are likely to be older, and since pregnancy will almost certainly place them at greatest risk, sterilization (or vasectomy of the partner) may be their best option.

*Congenital cardiac disease* refers to heart abnormalities and malformations such as septal defects, aortic and pulmonic valve stenosis, patent ductus arteriosus, aortic stenosis and Fallot's tetralogy present from birth. For women who have undergone surgical correction and have no ongoing cardiac disability the contraceptive choice should be unrestricted. For women with ongoing cardiac problems, the selection of the most appropriate contraceptive should be individualized, taking into account the risk of pregnancy, personal preference, the primary cardiac defect, surgical intervention and ongoing complications (1). In general, estrogen-containing contraception should be avoided but progestogen-only methods can be safely used.

#### NUROPSYCHIATRIC DISORDERS

Altered mood and depression have been reported by some women using hormonal contraception, particularly progestogen-only methods. There is a wide interindividual variation in mood changes, however, causation cannot be assumed. With the exception of progestogen only injectables, hormonal contraceptives can be quickly discontinued should mood changes occur (13).

Most of psychiatric disorders do not require special medical consideration concerning contraception.

*Chronic depression* is characterized by repeated episodes of severe depression without psychosis or mania. There is no good evidence to suggest that chronic depression is exacerbated by hormonal contraceptive use and that estrogen and progestogens interact with majority of antidepressants (1). Some treatments can induce liver enzymes and may reduce the contraceptive efficacy of some hormonal contraceptives (13).

Women with an *acute or severe psychiatric disorder* may have difficulty in making contraceptive choices and using methods which require strict compliance.

Sterilization is not recommended for men or women who have current psychiatric illness that may impair informed decision-making (4).

*Mentally disabled people* have the right to safe and healthy sexual life, but this right should be seen in conjunction with the rights of the care-givers for whom a pregnancy may be a burden and an eventual child's right to adequate parental care. There is a need to establish the ability of the client to make informed choice, to consider her/his ability to use the method consistently and correctly and to take care of their specific needs and problems. When the possibility of sterilization is contemplated for mentally disabled people who cannot make a decision by themselves, the decision should involve

the legal guardian and a team of professionals and should be guided by legislation (4).

Women with *convulsive disorders* can use any method of contraception. However, the anticonvulsants (phenytoin, carbamazepine, ethosuximide, phenobarbitone and primidone) may reduce the efficacy of hormonal contraceptives. For this reason, other methods are a better choice. With regard to the use of emergency hormonal contraception in this group of women, the standard regimen should be used (4).

Women should be asked about a history of *headaches* before starting COCs and every follow-up consultation. If a history of migraine is given, then women should be given clear advice about the symptoms that should be reported promptly (10). Focal migraine and migraine with aura are contraindications to the COC use. Other methods such as progestogen-only methods (pills, implants, Lng-IUS) or non-hormonal contraceptives can be recommended for such women. Progestogen-only injectables may not be considered, but only as the last choice, and should not be used at all if the woman has high blood pressure (4). Although the risk of ischemic stroke is very low in women of reproductive age, it is increased in women with migraine, particularly if they also take COCs (10). Women with migraine without aura (simple migraine): the onset or exacerbation of migraine or development of headache with a new pattern which is recurrent, persistent or severe requires discontinuation of the COC and evaluation of the cause (4). Absolute contraindication for COC use is migraine without aura if there is a history of more than one additional risk factor for ischemic stroke or migraine is treated with ergot derivatives (10). Progestogen-only contraceptives can be used by all women with any type of migraine (10).

#### LIVER AND BOWEL DISEASES

A non-hormonal method of contraception should be the first choice for women with liver disease. In those with active liver disease, *severe cirrhosis or liver tumor* estrogen-containing contraceptives are contraindicated. Progestogen-only contraceptives can be used but only as the last choice if other methods are not acceptable or not available. Those with *mild (compensated) cirrhosis* can use estrogen-containing contraceptives, but only as the last choice (4).

Women who are *carriers of hepatitis viruses* can use any hormonal method of contraception (4).

Women with *inflammatory bowel disease* should be offered unrestricted contraceptive choice. The absorption and efficacy of oral contraception is

unaffected in women with *colectomy and ileostomy*, but may be reduced in women with some bowel disease if there is malabsorption (particularly in *Chron's disease*). Evidence for this is limited. Hormonal contraception may be affected by drugs used in the management of inflammatory bowel disease. When the disease is severe and associated with hospital admission, dehydration, immobility or surgery, the risk of VTE increases. Use of estrogen-containing contraceptives in this situation needs to be balanced against the risk of VTE, which itself is increased with estrogen. Women with inflammatory bowel disease are more likely to develop osteopenia and osteoporosis than others, although the cause is unclear and the use of progestogen-injectable contraceptives should be considered carefully (1).

There are *two main ways in which drug intake may reduce the efficacy of COC*: induction of liver enzymes and effects on enterohepatic circulation. Induction of liver enzymes leads to an increase in metabolism and elimination of both estrogen and progestogen (this is most important with some anticonvulsants and rifampicin). Ethinylestradiol is a subject to an extensive "first-pass" metabolism. Glukuronide metabolites of ethinylestradiol are made in the liver, but once they re-enter the lumen of the bowel, the bowel flora are able to remove the glukuronide group and restore some ethinylestradiol for re-absorption and this may help

to maintain its level in the circulation. Certain broad-spectrum antibiotics can alter the gut flora and theoretically reduce the re-absorption of restored ethinylestradiol. This effect only applies for short courses antibiotic therapy or to a change in long-term antibiotic therapy, since antibiotic resistance develops after two weeks. Progestogenic metabolites, which are re-absorbed from the bowel are biologically inactive and thus broad spectrum antibiotics have no effect on the efficacy of progestogen-only pills (10,14).

## HAEMATOLOGICAL DISORDERS

*Iron deficiency anemia*: Oral contraceptives can reduce menstrual flow by half or more and women can benefit from either COCs or a Lng-IUS. By contrast, unmedicated and Cu-IUD may increase the blood loss volume during menstrual periods and this should be taken into account when a woman has pre-existing anemia. *Sickle-cell disease*: Pregnancy could be life-threatening. Effective contraception should be ensured. Any contraceptive method, including hormonal contraceptives may be used but long-lasting progestogen-only methods should be the first choice. *Thalassaemia* is not a contraindication for any method of contraception (4).

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## KONTRACEPCIJA KOD ŽENA SA MEDICINSKIM POREMEĆAJIMA

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### SAŽETAK

U ovom radu se razmatraju važne činjenice koje treba uzeti u obzir kada savetujemo ženu sa nekim zdravstvenim problemom pri izboru metoda kontracepcije. Restrikcija u izboru metoda nije uvek prisutna. Na osnovu naših informacija, žena treba da napravi vlastiti izbor. Neophodno je imati u vidu uticaj zdravstvenog stanja na izabrani metod kontracepcije kao i uticaj izabranog kontraceptivnog metoda na zdravstveno stanje žene. Na izbor utiče mogućnost interakcije lekova i neke dodatne okolnosti.

*Ključne reči:* kontracepcija, zdravstveni poremećaji