

## Contraceptive Choice in Pre-existing Medical Disorders

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### Abstract

*Contraceptive counselling is both art and science. It is still more challenging in women with pre-existing medical disorders. Is woman's hormonal journey controversial or beneficial? Oestrogen is contraindicated in many medical disorders. Progesterone-only contraceptives and novel delivery systems may change traditional risk and benefit profiles in women with comorbidities. Primary care physician should strive for overcoming the barriers for contraception which are prevalent in association with comorbidities.*

*Keywords: Contraception; Chronic medical disorders; Oestrogen; Progesterone; Counselling.*

Women with chronic medical problems face increase pregnancy related risks compared with their healthy peers. Planning pregnancy improves maternal and fetal outcomes, medical conditions can be stabilized, teratogens can be avoided and early antenatal intervention and surveillance can be instituted.

Reversible highly effective contraceptive methods allow optimal family planning. A focus on comprehensive patient counselling is paramount because of increase risks or efficacy changes associated with interaction of disease, therapy and contraception. Women with comorbidities may not receive adequate counselling on contraceptive methods. Comprehensive knowledge of the array of contraceptive methods will facilitate better patient counselling.

The safest and most effective forms of contraception should be offered to women with medical conditions. Contraception decision making should include consideration of the risks and benefits of a given method Vs the consequences of an unintended pregnancy. Patient counselling should focus on helping women understand the need for contraception while optimising their health for pregnancy.

In this article, we review the recent literature on contraceptive options in chronic medical disorders. We explore the role of health care provider to determine the patient's medical eligibilities and match her preferences and life style to an appropriate method for contraceptive benefits while

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### Introduction

Never before in history of mankind, has there been more need for limiting population growth. Number of human beings on the planet will exceed our supply of resources, unless the current growth trends are stopped and reused. Use of hormonal contraceptives have revolutionized the reproductive life of women who have exposure to teratogenic medications or exposure to hostile intrauterine environment. Unfortunately, some medical conditions also complicate the use of reliable contraception safely.

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minimizing the risk of unintended pregnancy. We capture the role of progesterone only contraceptives in chronic medical disorders when oestrogen is contraindicated. We highlight recent information on the effects of obesity on various contraceptive methods.

#### *Diabetes Mellitus*

COCs should not be used in diabetic patients with any of the following risk factors:

- 1) Hypertension
- 2) Smoking
- 3) Age greater than 35 years
- 4) Uncontrolled Hyperlipidemia
- 5) Cardiovascular complications related to diabetes
- 6) Thrombophilic predisposition

In such cases, a low dose progestin alone should be recommended.

According to WHO guidelines, the different types of combined contraception (COCs, patches, vaginal rings and injections) as well as progestin alone (oral, subcut. Implants, injectables and IUDs) are classified in category 1 for women with prior history of GDM.

MPA has been shown to decrease bone mineral density without altering carbohydrate tolerance, with an increase in levels of insulin and LDL cholesterol and a decrease in HDL cholesterol. Vaginal contraceptive ring, which releases constant amount of EE and Etonorgestrel, have minimal impact on CHO metabolism.[1]

Copper T 380A is rated by the CDC as safety category 1 (1=most safe to 4=least safe) for all patients with diabetes mellitus, regardless of severity of disease. The hormone-releasing LNG-IUS is also an excellent contraceptive choice for most women with diabetes mellitus, regardless of the severity of their diabetes or related comorbidities. Besides having a high safety rating, it also has high efficacy and patient satisfaction. With high intrauterine levels, but relatively low systemic levels of levonorgestrel, the LNG-IUS provides a dramatic reduction in menstrual blood loss

with relatively few hormone-related adverse effects.[2] Worsening of the control of carbohydrate metabolism or the lipid profile may contribute to vascular disease progression. One study compared the influence of levonorgestral-releasing IUD versus Cu IUD on carbohydrate metabolism in women who have type 1 Diabetes mellitus. No differences were found in daily insulin requirement, HbA1c levels, or fasting blood sugar after 12 months of use. Intrauterine contraception is safe and appropriate for women who have diabetes mellitus (Level A).[3]

#### *Obesity*

As the population becomes more obese over all demographic groups, increased attention has been turned to the safety and efficacy of various contraceptive methods for obese women. Increased body fat, as measured by body mass index, could affect steroid hormone metabolism because of increased basal metabolic rate, increased hepatic enzymatic metabolism or increased drug sequestration in fat. Higher pregnancy rates have not been observed among obese women using DMPA. Women of higher weight or body mass index were more likely to have contraceptive failures while using Norplant, levonorgestrel, subdermal implants.

Although the LNG-IUS produces low serum progestin levels, the intrauterine levels are 1000 times higher and provide the effective mechanism with regard to endometrial and cervical mucus changes. No increase in failure of the LNG-IUS by body weight has been noted. Several studies have provided evidence that low dose progestin-only and combined hormonal methods may be less effective in obese women. The authors estimated the attributable-risk from obesity is an additional two to four pregnancies per 100 woman-years. Although this is an important counselling point, clinicians should remember that the efficacy of COCs remains higher than that of barrier methods for obese women and that weight loss and consistent use should be

emphasized.

Obese women are at higher risk of venous thromboembolism than lean women. Women using estrogen-containing contraceptives are likewise at increased risk of venous clots. There is no evidence of increased venous thrombotic disease with progestin-only hormonal contraception. Although obesity decreases the efficacy of COCs, they are still likely to be more effective than barrier methods.[3]

Obesity can complicate the choice of contraception. WHO consider the benefits of OCPs in this population to be greater than the harm, although ACOG suggests that progesterone only method is safer. Weight has not been shown to change the effectiveness of the contraceptive ring or extended cycle OCPs. If the decision is made to prescribe OCPs to a patient who is obese, the physician should assess the co-morbidities that would preclude her from using OCPs, such as severe hypertension or uncontrolled diabetes mellitus.[4] Counselling obese patients should include mention of this moderate efficacy and the increased relative but small absolute risk of thromboembolism (Level B). The LNG-IUS may provide protection against pregnancy and obesity-associated endometrial hyperplasia (Level B).[3]

#### *Cardiovascular Diseases*

Cardiovascular diseases include various conditions such as coronary disease, rheumatic heart disease, cerebrovascular disease (stroke), thromboembolism and chronic hypertension. The IUD is an excellent and safe contraceptive for these women; however, meticulous aseptic care and prophylactic antibiotic at insertion time are needed to prevent bacterial endocarditis in those with rheumatic heart diseases. Combined pills are contraindicated in women with cerebrovascular or coronary disease, thromboembolism and severe hypertension. However low dose OCs including the triphasic pill can be used in mild hypertension, with no other additional risk factors such as smoking, obesity, diabetes or age over 35, but only under medical supervision. Progestin-only pills,

contraceptive patches and vaginal rings can also be used in this age group.(WHO 2004)

#### *Myocardial Infarction*

The risk of arterial thrombosis in relation to oral contraceptives (RATIO) study investigated the association between currently used oral contraceptives and myocardial infarction, according to the type of progestagen, oestrogen dose, and the presence of prothrombotic mutations. The overall estimated risk increased by about 2-fold relative to non-users. Among women with major classical risk factors for myocardial infarction who used low-dose oral contraceptives the risk was much higher. Since the identification of the factor V leiden mutation, which leads to resistance to activated protein C, it became clear that interaction between genetic and environmental factors, such as oral contraceptive use, plays a crucial role in the occurrence of thrombotic disease.

Smoking is by far the most important risk factor for myocardial infarction, therefore women should be encouraged to quit smoking. For women who continue to smoke, oral contraceptive use should not be continued after age 35 and an alternative contraceptive method should be recommended. In addition, combined oral contraceptive users with hypertension appear to be at increased risk of myocardial infarction and stroke relative to users without hypertension.

In recent epidemiologic studies the risk of venous thrombosis was found to be higher for third generation oral contraceptives than for second generation oral contraceptives, third generation oral contraceptives should not be the first choice in new users. Finally, a personal history of a thrombotic event is a contraindication for using oral contraceptives.[5]

#### *Hypertension*

Women with hypertension are at increased risk for cardiovascular events. Combined oral

contraceptive (COC) use, even among low-dose users, has been associated with a small excess risk for cardiovascular events among healthy women. The studies conducted by Kathryn M. Curtis and Anshu Mohllajee showed that hypertensive COC users were at higher risk for stroke and acute myocardial infarction (AMI) than hypertensive non-COC users, but that they were not at higher risk for venous thromboembolism (VTE). COC users were at higher risk for ischemic stroke and AMI, but not for hemorrhagic stroke or VTE. Combined oral contraceptive (COC) use, even among low-dose users, has been associated with a small excess risk for cardiovascular events among healthy women.[6]

According to WHO and CDC guidelines, women with controlled or uncontrolled hypertension should not be offered combined oral contraceptives, the patch, or the ring (Category 3-theoretical or proven risks outweigh the benefits and category 4 for systolic B.P. greater than 160 mmHg/ diastolic B.P. > 100 mmHg)

The progesterone-only pill (Minipill) medroxy progesterone acetate (im), Mirena (IUCD), the Cu IUCD and etonogestrel implants are all safe options.

A small subset of patients develop elevated B.P. after starting hormonal contraceptives, Oestrogen-containing hormones can increase the liver's output of angiotensin, which is a rennin-substrate that activates the renin-angiotensin-aldosterone system. If this becomes clinically apparent, these patients should refrain from Oestrogen containing products and use progestin-only formulations as a safer alternative.[7]

### *Thromboembolism*

Progesterone only pills are used mainly for women aged 35 yrs or more because the risk of thromboembolic disease is low than that with oestrogen-progestone preparations.

Although OCPs can increase the risk of VTE in all users, the risk is especially high in:-

1. Women with a history of VTE

2. Women with antiphospholipid syndrome
3. Women who are undergoing major surgery with an anticipated period of prolonged immobilisation.

The risk of VTE may also be higher in women who use OCPs that contain third generation progestins, such as desogestral and gestodine. The risks should be balanced with the risk of pregnancy and pregnancy related complications.[8]

While COC use by itself is a risk factor for VTE, results from the WHO Collaborative Study showed no effect of history of high blood pressure on the risk of VTE with COC use. The studies conducted by Kathryn Curtis and Anshu Mohllajee showed that hypertensive COC users were at higher risk for AMI and stroke than hypertensive non-COC users, but not at higher risk for VTE.[6]

The updated CDC guidelines for the use of hormonal contraceptives state that patients who receive anticoagulation for at least 3 months and who have no history of VTE or a low risks of recurrent VTE (No evidence of active cancer, no known thrombophilia) may use oestrogen containing contraceptives in select cases (category 3-theoretical risk outweighs benefits but not an absolute contraindication). Select patients may benefit from menstrual cycle control while receiving anticoagulation. However, other contraceptive alternatives are preferred if possible. Progestin-only treatment such as Mirena and the etonogestral implant (Implanon) are non-surgical options that may reduce menorrhagia and are safer alternatives for patients with thrombophilia.

The rate of VTE in O.C. users is estimated as 9 to 10 per 10000 women per year. However, rates of VTE associated with pregnancy and postpartum states are exponentially greater. In December 2011, an FDA panel voted that the benefits of Drospirenone-containing contraceptives, such as preventing pregnancy, outweigh the potential risk. Health care providers should engage patients in an informed decisions about

all risks and benefits of hormonal contraceptives and note this risk of VTE is higher in gravid women.[7]

### *Migraine*

Migraine in women of childbearing age significantly increases the risk of ischaemic but not haemorrhagic stroke. The coexistence of oral contraceptive use, high blood pressure, or smoking seems to exert a greater than multiplicative effect on the risk of ischaemic stroke associated with migraine. Oral contraceptives are known to be an independent risk factor for ischaemic and haemorrhagic strokes, particularly in patients who smoke, are aged over 35, or who have a history of hypertension. This risk is lower in women who use low dose (<50 µg oestrogen) rather than high dose (≥50 µg) contraceptives. Study conducted by C. L. Chang revealed an additionally increased risk of ischaemic stroke in migrainous women who also used oral contraceptives containing high doses of oestrogen (≥50 µg)

Low dose COCs can be given to women with simple migraine. However, these should be stopped if there are recurrent, persistent and severe attacks of migraine. Progesterone only contraceptives (pills, injections and implants) may also be used with caution in cases of migraine without aura. Cu-IUDs are most suitable for migraine with aura. (WHO 2004)(10). For this reason, migraine headache with aura is a contraindicator to combined hormonal contraceptives. OCPs may be cautiously considered in women who have migraine headaches, if they do not have focal neurologic symptoms (such as aura), do not smoke are younger than 35 yrs, and are otherwise healthy.[8]

Women with migraine who have focal neurologic symptoms or other risk factors for stroke (smokers, >35 yrs) should be counselled to use intra-uterine contraception, barrier methods, or progestin only contraceptives (Level B).[3]

### *Sickle Cell Disease*

Progesterone only (pills and implants) and

DMPA injections are suitable for such patients. COCs can be prescribed safely in the carrier state of the disease. COCs and IUCDs fall in WHO category 2 (adv. Outweigh risks). Advantage of depot medroxy is that it is associated with inhibition of sickling and improvement in anaemia in patients with sickle cell disease.[10]

### *Iron Deficiency Anaemia*

COCs reduce menstrual flow and hence are suitable for anaemic patients of course iron must be given too. CuTs mostly increase menstrual bleeding and cannot be used. Implants and injectable are suitable for anaemic patients.[9]

### *Hyperlipidemia*

Because low-dose oral contraceptives have negligible impact on lipoprotein profile, hyperlipidemia is not an absolute contraindication with the exception of very high levels of triglycerides (which can be made worse by oestrogen). If other risk factors are present, especially smoking, O.C. is not recommended. Dislipidemic patient who begin oral contraceptive should have their lipoprotein profile monitored monthly, for a few visits to ensure no adverse impact. If the lipid abnormality cannot be controlled, an alternative method should be used. O.C containing desogestral, noregestimate or gestodene can increase HDL levels, but it is not known if this change is clinically significant.[10]

### *Tuberculosis*

COCs should not be used by tuberculosis women who are being treated with Rifampicin. IUCDs can be used in non-pelvic TB. Condoms can be used by these cases. After cure COCs can be used.[9]

### *Epilepsy*

Hormonal contraception – Certain

contraceptives are rendered less effective by medication that induces hepatic glucuronide conjugating enzymes. Thus, women taking carbamazepine, phenytoin, topiramate or oxcarbazepine, who wish to take an oral contraceptive, would require a preparation containing at least 50 µg ethinylloestradiol, and even then should consider using additional barrier contraception. Levonorgestrel implants are occasionally ineffective in women receiving these AEDs, and medroxyprogesterone injections must be given every 10 rather than 12 weeks. Although lamotrigine does not promote hormonal contraceptive failure, lamotrigine concentrations may be lowered by the oral contraceptive, allowing possible breakthrough seizures or toxic effects on contraception withdrawal. Yuzpe regimen or LNG-only pills can be used for Emergency contraception.[11]

#### *Anticonvulsant Use*

When managing a patient on anticonvulsants, the physician must first determine which anticonvulsant she is using and whether an interaction occurs with hormonal contraceptives. Some patients may take more than one anticonvulsant medication. If a drug interaction exists, options include suggesting a higher dose pill (although it is important to explain the lack of good evidence strategy: Level C), recommending a second method for increased protection (e.g., condoms), or using DMPA, the levonorgestral intrauterine system (LNG-IUS), or a copper IUD (Level B). Implants and progestin only pills are not recommended because of their low systemic progestin levels.[3]

#### *Contraception in Psychological Disorders*

Proper counselling and informed consent of the patient or her legal guardian should be obtained. Patients who can use the contraceptive method consistently can avail of OCs or barriers, otherwise IUD is the method of choice. Sterilisation or even hysterectomy should be seriously considered for psychiatric women who cannot take care

of their own health.[12] Certain anti-psychotic medications decrease level of hormonal contraceptives by induction of CYP450 enzyme. Depot medroxy-P raises the seizure threshold by a mechanism attributed to high levels of progestin and is a better option for epileptic patients. Some evidence points to slight improvement of depressive symptoms after 1 year in patients who took depot-provera compared to those who discontinued drug.[7]

#### *Systemic Lupus Erythromatosus*

SLE is common in reproductive age women. Evaluating acceptable contraceptive methods for women who have SLE requires consideration of:

- 1) Possible increased risk of thrombosis caused by vasculitis and prothrombotic antibodies.
- 2) Immunosuppression caused by long term steroid use.
- 3) Possible exacerbation of disease flares or progression by contraceptive agents.

Many clinicians are leery of using intrauterine contraception in women who are currently or potentially immunosuppressed, such as women who have SLE. Another theoretical concern is whether immunocompetence is required for efficacy of copper IUCDs. In a study conducted by Stephanie B. Teal and David M. Ginosar, there were two cases of copper IUCD failure in renal transplant patients. The US Food and Drug Administration recently removed immunosuppression as a contraindication to Cu IUCD use. For women who have lupus and take anticoagulant medication because of history of thrombosis or antiphospholipid antibodies, the levonorgestral IUCD especially appropriate to control menstrual blood loss.

DMPA has not been as carefully studied for women with lupus. Benefits include excellent contraception with no increased risk of thrombosis and no apparent increase in disease activity, although the data is limited. Risk include bone loss in women who are

already at risk for significant osteopenia if on longterm steroids, such as prednisone.[3]

Use of OCPs in women with stable or inactive SLE does not appear to increase mild or severe flare ups. If vascular disease, nephritis or antiphospholipid antibodies are present progesterone only method is more appropriate.[4]

### *Counselling*

Effective contraceptive counselling requires an history, as well as the risks, benefits, adverse effects, and contraindications of each method. Empowering and educating our patients about their body's hormones, the menstrual cycle and the risk of unintended pregnancy are central to effective contraceptive counselling.

### *Barriers to Contraception*

Barriers to contraception still exists ranging from various insurance coverage to healthcare access to difficulties with use of various methods. Another barrier is physician's lack of up-to-date knowledge about contraceptive methods. Woman's perceived lack of control over her ability to avoid pregnancy is an additional barrier to contraceptive use and compliance. Further research will need to investigate how much attitudes can be approved and addressed in family planning messages.[5]

## **Discussion**

Advances in medical care have allowed women with various medical conditions to have quality of life unthinkable 50 yrs ago. Even women who are debilitated by disease can be at increase risk of pregnancy. Women who would have been counseled to consider sterilisation in the past, such as women who have type1 DM, HIV infection, or lupus currently look forward to healthy pregnancies with careful control of their conditions before and during pregnancy. Although there may be no risk-free contraceptive choices, unplanned or mistimed pregnancy is riskier.

Having a chronic medical condition influences how women think about future pregnancy; however knowledge and attitude about pregnancy varies by specific medical conditions. Women are not fully aware of potential reproductive health and pregnancy related risks of their chronic condition, which may lead to uninformed decisions about future pregnancy, pregnancy avoidance, and pre-conception planning. Current clinical practice and research is aimed at pre-conception health promotion in reproductive age. Women with chronic conditions should address these gaps in knowledge to achieve the goal of avoiding unintended pregnancy outcomes.

There is much work still to be done before ideal contraceptive technology can be developed and made universally available. Selecting an appropriate method for a patient and her medical profile is rewarding and challenging in view of new medications, novel delivery systems and evolving research.

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