

# Hormonal contraception in women with autoimmune diseases

## Abstract

Hormonal contraception represents the contraceptive method of choice for the majority of women aged between 15 and 44 from developing countries. The majority of autoimmune diseases, especially rheumatologically ones, as systemic lupus erythematosus (SLE), rheumatoid arthritis, polymyositis or dermatomyositis, scleroderma or Sjogren syndrome, mainly affects the female population. Early counseling of these patients on the existing contraceptive methods is particularly important for several reasons: women with autoimmune diseases have the same infertility rate compared to healthy women; the treatments used for the basic disease can present adverse fetal effects; if pregnancy coincides with the disease remission, the odds for a healthy pregnancy and devoid of adverse events increases. Women with autoimmune diseases have the same need to choose a safe and efficient contraceptive method just like general population. Physicians should fully understand the advantages and disadvantages of each contraceptive method, the effect of various contraceptive methods in disease activity, health risks, and the possibility of interaction with other competing drugs as well as the couple's preferences. Combined oral contraception is efficient, convenient and reversible. These have indication in most of autoimmune pathologies including SLE, outside of flares, in the absence of antiphospholipid syndrome or other thrombotic risk factors. In this review, we tried to summarize the instructions for using hormonal contraception by women at reproductive age, affected by one of the main autoimmune diseases, conditions with an important component in young female population.

**Keywords:** contraception, lupus erythematosus, rheumatoid arthritis, diabetes mellitus

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## Introduction

Hormonal contraception, properly used, has represented from the beginning, the most convenient and effective non-surgical contraceptive method, having an acceptable safety profile. Thereby, hormonal contraception represents the contraceptive method of choice for the majority of women aged between 15 and 44 from developing countries<sup>(1)</sup>.

The majority of autoimmune diseases, especially rheumatologically ones, as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), polymyositis or dermatomyositis, scleroderma or Sjogren syndrome, mainly affect the female population. A sizeable proportion from these patients is of reproductive age<sup>(2)</sup>. On the other hand, in spite of the associated autoimmune pathology the fertility is preserved in most of the patients. Therefore, early counseling of these patients on the existing contraceptive methods is of particular importance for several reasons: women with autoimmune diseases have the same infertility rate compared to healthy women; the drugs used in treating the basic disease can present adverse fetal effects; if pregnancy coincides with the disease remission phase, the odds for a healthy pregnancy and devoid of adverse events increases. At the same time, the lack of a reproductive health education program in schools represents one more reason why family planning is essential in rheumatological practice<sup>(3)</sup>.

The female predisposition to autoimmune and rheumatological diseases may have as a cause the invol-

vement of estrogen. It has been demonstrated that estrogen enhances the phagocytic activity of the macrophages, promotes maturation of T-helper cells and activates the polyclonal B cells<sup>(4)</sup>. Therefore, the use of estrogen containing products such as combined hormonal contraceptives would theoretically worsen these conditions, raising concerns among the doctors who counsel these patients, causing avoidance of recommendation for hormonal contraception in women with autoimmune diseases, particularly for those suffering from SLE, despite the effective and reversible protection, if a pregnancy is desired<sup>(5)</sup>.

The present review tends a rundown of instructions in using hormonal contraception in association with the main autoimmune diseases, RA, SLE, antiphospholipid syndrome (APS), inflammatory bowel disease or diabetes mellitus (DM), conditions with an important component in women at a reproductive age.

## Rheumatoid Arthritis

RA is an autoimmune condition characterized by joint swelling, with a female/male ratio of 2-3/1, and it associates chronic pain and invalidity, bone erosions, with a high risk for infections, but also for cardiovascular diseases<sup>(6)</sup>. Pregnancy diminishes, even abolishes symptoms in patients with RA, although these reappear in 90% of cases after birth<sup>(7)</sup>, suggesting a certain hormonal dependency regarding the disease's activity. Previous studies revealed that women who used combined

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oral contraceptives (COC) didn't develop RA or severe forms of RA<sup>(8)</sup>, while another studies showed that COC didn't present a protective effect in developing RA<sup>(9)</sup>. Withal, RA is a condition mediated by Th1 cytokines; therefore exposure to high levels of estrogens improves theoretically disease's activity<sup>(4)</sup>. Determination of contraceptive safety for women with PR is important because the onset of the disease appears in most cases at the reproductive age. Even more, some treatments for RA, as methotrexate, have teratogenic effects, and for sexually active women an efficient contraception is needed. On the other hand, the effect of hormonal contraception on the bones can't be neglected, the loss of bone mass being a severe complication of RA.

### Hormonal contraception in patients with RA

#### Estrogen based contraception

Information concerning the safety of COC for patients with RA is limited. Most of the studies have been published before 1970, patients being treated with much higher doses of hormones compared to nowadays. In addition, some studies used doubtful diagnostic tests for RA, so that we can't compare the improvement or the worsening of the disease in these or between these studies<sup>(10)</sup>. Five studies conducted on this topic, three of them before 1970, showed that COC had no effects on disease progression, while some of them showed an improvement of the symptoms<sup>(11-14)</sup>. A recent systematic analysis concerning the safety of hormonal contraceptive in women suffering of RA showed a tendency in improving the symptoms of RA, both objective and subjective<sup>(5)</sup>.

This information shows us that the worsening of progression in RA is unlikely when COC are used. There couldn't be found studies which can highlight other effects on women's health with RA and who use COC, including cardiovascular diseases, even if it is known that women at a reproductive age with RA are exposed to a 3-4 times higher risk to confront with a cardiovascular event compared with women without RA<sup>(6)</sup>.

#### Progesterone based contraception

Conducted studies show the fact that women with rheumatological conditions can safely use progestin only as contraceptive method to avoid pregnancy. These can be found in many forms: progestogen only pills (i.e. mini pill, POP), intramuscular injection every three months, a contraceptive implant for 3 years, an intrauterine device or emergency contraception. Progesterone doesn't seem to increase the immune system's activity and it is not associated with the increase of flares<sup>(15,16)</sup>. Even more, the progesterone doses used in these contraceptive methods does not increase the risk of thrombosis. It has been demonstrated that the use of depot-medroxyprogesterone acetate is associated with a decrease of bone mineral density<sup>(17)</sup>. Its clinical significance is uncertain in patients with RA and its recommendation must be individualized.

#### Recommendations

Taking into account that current studies demonstrate the lack of a negative effect of hormonal contraception

on RA progression, there shouldn't be existing contraindications in using this kind of contraception in women with RA. Currently, there is no data concerning the use of other forms of hormonal contraceptives in women with RA<sup>(18,19)</sup>.

### Systemic lupus erythematosus and antiphospholipid syndrome

Both SLE and APS affect predominantly young women, thus the importance of an adequate contraception. Contraception in women who suffer from SLE/APS outweighs the bare necessity to avoid unwanted pregnancies. There are some situations when an efficient contraception is required, such as early stage of disease, intense disease activity ("flares"), severe organ involvement, use of drugs with fetal toxicity or teratogenic potential. Even more, estrogenic pill is generally contraindicated in women with SLE. The message that should be understood it's that women with SLE can be considered good candidates for many contraceptive methods, the suitable method having to be individualized<sup>(20)</sup>.

Hormonal methods include oral contraceptives (COC or POP) and subcutaneous device. The use of COC was discouraged because of the role of estrogens in SLE pathogenesis<sup>(21)</sup>. However, two recent randomized studies<sup>(22,23)</sup> support the safety of using microdosed COC in patients with inactive or stable SLE. On the other hand, presence of APS remains a major contraindication of using COC because of the thrombogenic risk. Progesterone only based products (i.e. oral pill, medroxyprogesterone deposit, subcutaneous implant) don't seem to increase the immune system's activity, they are not associated with a high rate of exacerbations and they do not increase the risk of thrombosis; a recent study realized in patients with SLE showed a good gynecological tolerability (a low rate of interruption because of the bleeding or hypoestrogenism)<sup>(24)</sup>. A major concern regarding progesterone use, can be its effect on bone system. However, low bone mineral density proved to be reversible after treatment's interruption<sup>(25,26)</sup>.

### Systemic lupus erythematosus

SLE is an autoimmune disease that affects about 1 to 1000 persons with a ratio of 15:1 for women at reproductive age<sup>(27)</sup>, characterized by remissions and relapses. There are three forms of SLE according to its evolution: relapsing-remitting (recurrent exacerbations), chronic active (persistent active disease for a year) and subclinical (without clinical activity for a year). The first two are the most commonly found compared to the third<sup>(28-30)</sup>. Due to the frequency of the chronic active pattern, generally it is even more important to evaluate the disease's activity and not only the characteristic elements of flares. Estrogens and pregnancy modify the production of Th1/Th2 cytokine balance in favour of Th2. Therefore, the theoretical tendency of worsening appears if tissues have a high content of estrogens<sup>(4)</sup>.

Over time, pregnancy has been disheartened in women affected by SLE, because it is considered that the disease worsens during the pregnancy, exposing the mother and the fetus at a high risk. In the last 30 years, this condition's management has been improved, and with this also the approach with regard to a possible pregnancy. Patients with SLE can have successful pregnancies as long as its timing and management are carried out in close contact with qualified medical personnel<sup>(30-32)</sup>.

### Antiphospholipid syndrome

APS is an autoimmune acquired thrombophilia predominantly affecting young women. It can be primary or secondary if associated with SLE. Although SLE and APS may coexist in some patients, these are two distinct diseases. APS pathology is characterized by elevated levels of antibodies like: lupus anticoagulant, anticardiolipin, and clinical being characteristic thrombosis (i.e. arterial or venous), recurrent pregnancy loss and thrombocytopenia<sup>(32-36)</sup>.

APS may present as a primary form, without any systemic autoimmune basic disease, such as SLE. These kinds of patients present a high risk for obstetrical complications or recurrent pregnancy loss<sup>(28,37)</sup>.

### Hormonal contraception

Women diagnosed with SLE are often advised to quit COC<sup>(38,39)</sup>. The effect of oral contraceptives on the incidence and activity level of SLE has been a very debated research topic<sup>(40,41)</sup>. COC prescription should be taken into consideration in patients with SLE for several reasons. First of all, scheduled pregnancies during periods of remission have better results. At the same time, most women would appreciate a convenient contraceptive method like COC. Some studies reported a high frequency of exacerbations during pregnancy, which suggests a potential effect of estrogens in mediation of disease activity<sup>(31)</sup>. On the other hand, another studies didn't report worsening of the disease during pregnancy<sup>(42-46)</sup>.

There are conflicting data concerning the association between SLE onset with COC consumption. Nurses' Health Study revealed a high risk in developing SLE associated with COC use in the past<sup>(47,48)</sup>. A large study conducted among 786 women and 7814 control patients proved the existence of increased risk of SLE association with COC use<sup>(49)</sup>. Even more, Carolina Lupus Study, which followed up patients from the moment of diagnosis, did not show any association between SLE and COC use<sup>(50,51)</sup>.

COC have been associated with an increased number of flares, with variable severity. Other clinical elements with a high incidence among patients with SLE are thrombotic events. These can be enhanced by using COCs, and many studies approached these problems<sup>(1)</sup>. The Safety of Estrogen in Lupus Erythematosus National Assessment is a randomized study, double-blind with a group of premenopausal women

treated with COC and another with placebo. There haven't been noticed any flares in patients treated with COC compared with those with placebo, and the rate of discontinuation due to various reasons (i.e. secondary effects, pregnancy, volunteer etc.) has been similar between groups<sup>(35)</sup>. Two randomized studies, placebo controlled, discovered that estrogen containing pills have not increased the number of exacerbations in women with stable SLE, mild form<sup>(46,47)</sup>. These studies have not included women with flares because the assessment of these preparations is prohibited during periods of disease activity. Therefore, randomized studies demonstrate the safety of using microdosed COC in patients with inactive or stable form of SLE, in terms of risk to trigger an exacerbation. On the other hand, large case-control studies suggested that incidence of SLE is increased during COC use and not because their use in the past. The risk is higher in patients using second generation preparations or with high doses of hormones<sup>(44,45)</sup>.

On the other hand, increased level of estradiol can cause thrombosis in predisposed women, making these drugs contraindicated in individuals with positive antiphospholipid antibodies (APA). Women with SLE have a 3X higher risk of thrombosis compared with general population, making estrogen a risky contraceptive method<sup>(3)</sup>. Thus, in women who take into consideration the use of estrogen containing products, it is very important to determine the presence of APA. APA are frequently met among patients with autoimmune diseases, especially SLE. Women with positive APA are predisposed to venous and arterial thromboembolism; therefore estrogen containing contraceptives are contraindicated in these women<sup>(52-55)</sup>.

Data on cardiovascular outcomes are more limited. Only two studies have examined specifically thromboembolic events, both of them including only women with positive APA<sup>(56,57)</sup>. In these studies, a tendency to a positive correlation between COC use and thromboembolism is present, especially arterial, that indicates an increased probability for a thrombotic event in women with positive APA and with a history of COC use.

Association between high doses of estrogen and venous thromboembolism is recognized for several decades, and some studies shows that both estrogen and progesterone are thought to be involved in arterial thrombosis pathogenesis. Recent studies suggest that microdosed products and second generation progestative products are not associated with increased risk of cerebrovascular diseases. These progestins are thought to have fewer adverse effects on clotting mechanisms, while the third generation progestogens have been shown to cause thromboembolic events. Incidence of thrombosis in women who use hormonal contraceptives is more increased if there is already a predisposition to thromboembolic diseases such as acquired or congenital thrombophilia<sup>(43)</sup>.

Association between COC and thrombosis in young women represents a subject of interest and the type



of used progestin seems to be particularly important in the incidence of venous thromboembolism. Third generation of progestogen containing products is considered to be the most thrombogenic. Thrombosis in young women that use COC creates the suspicion of thrombophilia, so that many women with APS are diagnosed in this way. Some studies didn't report any increase of the incidence of thromboembolic disease in women with APS that used microdosed COC. On the other hand, there is no information on the use of POP in women with APS and the risk of thrombosis<sup>(43)</sup>.

Lakasing et al. suggest that COC used by women with APA doubles the incidence of thrombosis. Regarding other forms of contraception, authors believe that POP are not associated with unusual side effects, although very few women have used this form of contraception<sup>(43)</sup>.

As for other effects of COC in patients with SLE, it is known that women with SLE have an increased risk of fracture, with maximum statistics significance among women aged between 18-24<sup>(58,59)</sup>, and available data from studies conducted on two cohorts with SLE have shown that the use of COC gives protection in terms of musculoskeletal injuries in SLE: decreases the risk of musculoskeletal damage in Hopkins Lupus Cohort and decreases the number of fractures in the study conducted by Ramsey-Goldman et al.<sup>(58,59)</sup>. Although these studies are limited due to the lack of specific information on the type, duration and form of used COC, it is important to take into account the potential benefits of contraceptive methods, as well as the risks to which they expose women with SLE.

All these data suggests that the association between use of COC and lupus flares is weak. On the other hand, the decision to use COC in patients with SLE should take into consideration the presence of APS. Other risk factors for thrombotic events recognized in the general population, such as tobacco use, venous insufficiency or other thrombophilic defects should be also considered in patients with SLE<sup>(1)</sup>. Women with APS should be advised firmly against using this form of contraception. This advice should be applied for both second and third generation of progestogen containing drugs<sup>(43)</sup>.

## Recommendations

Based on the results from these studies, World Health Organization (WHO) has recently added new guidelines concerning the use of contraceptive methods in patients with SLE. Shortly, the use of any form of hormonal contraceptive may be indicated in SLE, when there are no flares, with the exception of patients who have positive or undetermined APA. In women with APS any form of hormonal contraception is absolutely contraindicated and the use of POP has a relative contraindication. Even more, women with LES can have coexistent cardiovascular risk factors which should be taken into consideration when the use of hormonal contraceptives is wanted<sup>(60)</sup>.

Despite all risks, the use of COC has brought benefits to patients with SLE such as control of pregnancy and

delivery and maintenance of ovarian function in patients with SLE receiving cyclophosphamide. For these reasons, the use of COC should be taken into consideration in patients with SLE and the decision must weigh the benefits and the risks for each patient<sup>(1)</sup>. Therefore, in patients with SLE, hormonal contraception should be taken into consideration if: there are not relative or absolute contraindications as in the general population, inactive or stable/mild SLE, the absence of arterial or venous thromboembolism in the past, the absence of APA, non-smoker, normotensive. For COC, it is recommended to use the lowest dose of etinil-estradiol. POP should be taken into consideration<sup>(1)</sup>.

Available data indicates that many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives. Women with positive APA have a significant risk of arterial and venous thrombosis and, therefore, the use of some combined hormonal methods should be avoided in these women. Even more, patients with SLE are more susceptible to certain co-morbidities, such as thrombocytopenia, severe atherosclerosis, arterial hypertension and venous thromboembolism, which can make some contraceptives less recommended. Further studies of contraceptive methods are needed, other than oral methods in women with SLE. On the other hand, generally, the benefits of contraceptives for many women with SLE surpass the risks of an unwanted pregnancy<sup>(61)</sup>.

## Diabetes mellitus

The prevalence of DM, type 1 or 2, is increasing obviously worldwide, affecting more women of reproductive age, with a percentage of 2 among persons aged between 18-44. DM is associated with a high risk of congenital malformations, perinatal mortality and spontaneous abortions<sup>(62,63)</sup>. These concerning epidemiologic considerations show that pregnancy would increase the risk of complications for both mother and fetus. Moreover, current medicine faces a growing number of complex situations, such as teenagers with type 1 DM, poorly controlled, or young women with type 2 DM associated with obesity and concomitant cardiovascular risk factors<sup>(64)</sup>.

On the other hand, preconception health optimization demonstrates an improving of pregnancies results in patients with diabetes<sup>(65)</sup>, highlighting the importance of avoiding unwanted pregnancies and the promoting of pregnancy planning. It was found that 70% of women with DM, with unplanned pregnancies, used contraceptives in less than half of the cases, mainly because of the misconception of association of diabetes with infertility<sup>(66)</sup>.

There is controversy about the use of contraception in women with diabetes. Frequently, they follow different strategies that are neither effective nor safe, resulting in an unwanted pregnancy<sup>(67)</sup>. It is now recognized that hormonal contraception is a safe and effective option for women with uncomplicated diabetes. There

are still a significant number of young women with poorly controlled diabetes, or with other risk factors like cardiovascular diseases, that determine health professionals to avoid the use of hormonal contraceptives. As a paradox, these women have the highest risk of unplanned pregnancy. Women with diabetes may choose the same contraceptives like general population, although the potential metabolic effects of the contraceptive methods may require a risk/benefit assessment, the main concern especially referring to macro-vascular complications, such as cardiovascular diseases<sup>(68)</sup>.

It seems that both women and health professionals avoid COC because of concerns of adverse metabolic and cardiovascular effects<sup>(69)</sup>, although studies that involve microdosed COC did not present proves of diabetes metabolic impairment<sup>(70,71)</sup>. However, in older women, with type 2 diabetes and risk factors like cardiovascular diseases (i.e. smokers, insulin users, etc.) caution is needed when estrogen contraceptives are used<sup>(68)</sup>. It is recommended that these women postpone pregnancy until they reach the optimal control of glucose and/or stabilization of microvascular complications, such as retinopathy. This absolute need for planning the pregnancy emphasizes once again that the proper use of contraceptives represents a crucial step in managing diabetes in women of reproductive age<sup>(65)</sup>.

### Hormonal contraception

In women with DM, one of the most important aspects related to the potential effect of hormonal contraceptives on the occurrence or progression of degenerative complications, especially retinopathy or glomerulopathy, because of the microvascular circulation's damage. On the other hand, another important aspect regarding hormonal contraception use is represented by their metabolic effects, referring especially to glycemic control. The conducted studies did not find any difference in daily insulin requirements, in glycosylated hemoglobin level or in à jeun glucose level, after 12 months of contraception in women with type 1 diabetes. Moreover, analyzing the entire diabetic population, no changes in blood glucose levels have been reported following the use of several methods of contraception. Only the use of high doses of COC has negatively affected glucoses homeostasis<sup>(72)</sup>.

Regarding the degenerative complications, there have not been reported any increases in prevalence and/or of the severity of microvascular complications (i.e. retinopathy or nephropathy) in women with type 1 diabetes that used COC. Moreover, they didn't exert a negative effect on the progression of retinopathy or on the incidence of macular edema in diabetic women with early-onset diabetes (type 1) or on DM which debuted at an older age (both type 1 and type2)<sup>(73)</sup>.

On the other hand, the safety of oral contraceptives should be analyzed according to the cardiovascular risk, especially in women with type 2 diabetes. This disease is often associated with obesity and multiple

cardiovascular risk factors, such as arterial hypertension and dyslipidemia. There is no data or study specifically dedicated to women with diabetes focused on cardiovascular safety of COC, available results driving only from subgroups of analysis. Identifying one or more cardiovascular risk factors in combination with DM should determine reservation in prescribing COC. Also the potential worsening effect of COC on cardiovascular risk factors in women with diabetes is important. This type of contraception modifies the plasmatic lipid profile, causing elevated triglycerides, low-density lipoprotein-cholesterol and a slight decrease in high-density lipoprotein-cholesterol, according to the estrogens dose and to the androgenic action of the progestogens<sup>(74,75)</sup>. In clinical practice, lipid profile should be analyzed before and followed up after COC initiation. Moreover, COC should be contraindicated in case of persistent hypertriglyceridemia in patients with diabetes. In the absence of familial dyslipidemia or of nephropathy, in patients with type 1 DM, the status seems to be quite different, as there are not significant changes in insulin sensitivity, in lipidic profile or in coagulation parameters after starting a COC compared to non-diabetic women<sup>(76)</sup>. Another aspect relates to the increased risk of thromboembolic events in diabetic women. Although vaginal or trans-dermic administration of estrogen-progestogen combinations limits the influence on liver protein synthesis, the safety of these routes of administration has not been evaluated so far and contraindications remain the same as those for COC in diabetic women. Also, the safety of using hormonal contraceptives containing estradiol valerate or 17-beta estradiol has not been evaluated in women with diabetes<sup>(62)</sup>.

A recent study supports that the use of injectable contraceptives like Depo-Provera and POP is preferable in women with diabetes because of smaller risks associated with cardiovascular diseases. On the other hand, there shouldn't be forgotten that prolonged use of Depo-Provera is associated with low bone density, and women who use this method should be monitored, especially if there are other risk factors for osteoporosis. In these situations, alternative methods of contraception are preferred<sup>(77,78)</sup>.

### The use of oral contraception in women with diabetes

As mentioned earlier, it is essential to take into consideration the presence of microvascular damage or of some cardiovascular complications with or without vascular risk factors (i.e. dyslipidemia, arterial hypertension, tobacco consumption, diabetes for more than 20 years) before prescribing any type of COC in women with type 1 DM. COC may be prescribed in women with type 1 diabetes that don't have microvascular or macrovascular complications, as well when no cardiovascular risk factor exists<sup>(62)</sup>. Inadequate glycemic control alone is not a contraindication for COC use, but a special attention must be directed to the associated risk factors,

especially tobacco use. If degenerative severe complications are present, as nephropathy with proteinuria with or without kidney failure, active retinopathy (i.e. ischemic or proliferative area), cardiovascular diseases or peripheral/vegetative neuropathy, COC should be contraindicated. Because of the vascular safety and because of the reduced metabolic effects, POP represents an efficient alternative<sup>(62)</sup>.

The use of COC should be restricted in women with type 2 diabetes, and choosing an alternative contraceptive method, such as POP or those non-hormonal should be considered systematically<sup>(62)</sup>. The incidence of type 2 diabetes increases fast in women, in association with overweight or obesity, but in absence of additional vascular risk factors, young women being the most affected. COC may be proposed in these cases, but only in women without obesity, without additional cardiovascular risk factors, microvascular or cardiovascular complications<sup>(62)</sup>.

## Recommendations

Available data suggest that COC represents a safe and efficient option for family planning in women with diabetes, at least for those with uncomplicated forms of diabetes. Recent recommendations showed the necessity of avoiding estrogen-progesterone contraceptives in case of associated cardiovascular risk factors, cardiovascular diseases or severe microvascular complications, such as nephropathy with proteinuria or active proliferative retinopathy.

Nowadays, the number of women with type 2 diabetes of reproductive age is much higher and COC should be used with caution in this group of population due to frequent association of obesity and the presence of vascular risk factors that increase the rate of thromboembolic events and arterial risks<sup>(62)</sup>.

For women with diabetes who need hormonal contraception, a safe method is needed, reported to adverse reactions risk and diabetes complications. WHO has established criteria for medical eligibility to help the

assessment of these risks, and health professionals who advise women with diabetes should be aware of the range of the available contraceptive options and of their related risks, to prevent unplanned pregnancies<sup>(74)</sup>.

## Take home messages

Diabetic women are exposed to numerous complications during pregnancy. Diabetic women have a low probability to use contraceptive methods, especially COC compared to non-diabetic women. COC represent a safe and efficient option in women with DM, at least for those with uncomplicated DM. POP represents an alternative that should be taken into consideration in case if other cardiovascular risk factors are associated, cardiovascular diseases or severe microvascular complications.

## Conclusions

Women with autoimmune diseases (i.e. SLE, APS, DM etc.) have the same need to choose a safe and efficient contraceptive method just like general population. Physicians should fully understand the advantages and disadvantages of each contraceptive method, the effect of various contraceptive methods in disease activity, health risks, and the possibility of interaction with other competing medicinal products as well as the couple's preferences. COC are efficient, convenient and reversible. These have indication in most of the autoimmune pathologies including SLE, outside of flares activity, in the absence of APA or of other thrombotic risk factors. For women in whom estrogen containing hormonal products is a concern, POP can be considered.

However, the principles of prescribing hormonal contraceptives for the general population should apply also to women with autoimmune diseases. These should be always revised in the context of comorbidities and other risk factors that favour or contraindicate use of hormonal agents. Through this, the balance between benefits and risks can be properly assessed and compared to all other available treatment alternatives. ■

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