

Hormonal contraception and risk of sexually transmitted disease acquisition

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Abstract

Worldwide, an increasing number of women are deciding to use hormonal contraception. This review presents the current knowledge of the effect of this contraceptive method on the risk of sexually transmitted disease acquisition. Several studies suggest that hormonal contraception users are at increased risk of sexually transmitted diseases. However, many other studies did not demonstrate it. It is proved that using hormonal contraception may have a protective effect on bacterial and trichomoniasis infection. Moreover, the risk of infection is positively associated with the composition of hormonal contraception and women's lifestyles.

Key words: hormonal contraception, infection, sexually transmitted disease.

Introduction

In the whole world millions of women use hormonal contraception as a method of pregnancy planning. Therefore, the method should be totally safe, effective, cheap and offer an opportunity of fast return to fertility after discontinuation of the contraception, and should not be directly related to a sexual act. However, many hormonal contraceptives have a direct and indirect influence on the susceptibility to sexually transmitted infections [1-4]. Unfortunately, there is little information in the available literature on the potential risk of sexually transmitted infections in women using this type of contraception.

Aim of the study

The aim of the study was to present the current state of knowledge on the influence of hormonal contraception on development of sexually transmitted infections.

Types of hormonal contraception

There are two types of hormonal contraceptives: 1) contraceptives with oestrogens and progestagens, and 2) contraceptives containing only progestagens (Table 1).

Oestrogens in the first half of the menstrual cycle decrease the FSH synthesis by the anterior lobe of the pituitary gland, which consequently prevents follicles from maturing and ovulating. On the other hand, gestagens in the second half of the cycle prevent implantation of an ovum in the uterus by inducing the secretory phase of the endometrium and causing changes in the composition of cervical mucus and decreasing its permeability to spermatozoa (Table 2).

Every decision about the use of hormonal contraception must be adapted to the needs of a patient and her current state of health. A proper choice of a preparation should consider not only the effectiveness, advantages and disadvantages of a preparation, but also other factors, such as education and knowledge of a patient, scrupulousness in medicine administration, type of sexual activity (sporadic or regular), and also religious and economic issues. Moreover, also the influence of contraceptives on potential infections (including sexually transmitted infections) is of great importance. It should be borne in mind that the use of hormonal contraception requires absolute observance of contraindications, which include the following: actual or suspected pregnancy, high risk of vascular disease, past thromboembolic disease,

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Table 1. Types of hormonal contraception [5-8]

	Combined oral contraceptives	Contraceptive patches	Mini-pills	Progestagen injections	Intra-uterine hormonal system	Contraceptive rings
Administration	PO daily	Transdermal every 7 days	PO daily	IM every 3 months	Intrauterine every 5 years	Transvaginal every 4 weeks
Composition – the dose of oestrogens and gestagens	Low/low	Low/low	0/very low	0/high	0/low	Low/low
Inhibition of ovulation	+++	+++	+	+++	+	+++
Cervical mucus: decrease in permeability to sperm	Yes	Yes	Yes	Yes	Yes	Yes
Endometrium: decrease in the ability to accept a blastocyst	Yes	Yes	Yes	Yes	Yes	Yes
Mean time between contraception discontinuation and fertilization [months]	3	3	2	6	1-2	3

PO – per os, IM – intramuscular

varicose veins of extremities, valvular heart disease associated with pulmonary hypertension and thrombosis, arterial hypertension, ischaemic heart disease, active liver disease, porphyria, cholelithiasis, recent gestational trophoblastic disease, and breast and uterine cancer [7, 8].

All of the methods of hormonal contraception have similar side effects resulting from delivering a dose of hormones to an organism. These are nausea, headache, mastalgia, change in body weight, decrease in libido and mood swings tending toward depression. Their intensity is different in various types of contraception. However, they are the most evident in the use of combined oral contraceptives (COC) [5-8].

Sexually transmitted infections

Sexually transmitted infections remain a great health problem of hetero- and homosexual groups alike. Bacteria, fungi, viruses and protozoa can be transmitted by sexual activity. Some of them may cause infections limited to the urogenital system, while others may also result in infections of other organs, and in intrauterine and perinatal infections. The most frequent sexually transmitted diseases include the following:

- chlamydial infections,
- genital herpes,
- HPV infections,

Table 2. Advantages and disadvantages of different types of hormonal contraception [5-8]

Type of contraception	Advantages	Disadvantages
COC	– Reduction of risk of ectopic pregnancy, ovary cancer, uterine cancer, benign breast diseases, ovarian cysts, uterine myomas, pelvic inflammatory disease	– Interactions with medicines – Negative effect on lipid and carbohydrate metabolism – Increased risk of thromboembolic and cardiovascular diseases
Contraceptive patches	– The same as in COC – Lower doses of hormones than in COC – Comfortable use	– Possible detachment, skin irritation – Interactions with medicines – Contraindicated in obese persons
Mini-pills	– Good tolerance – Minimum influence on lactation – Little metabolic changes	– Very regular administration is required – Irregular menstruations – Higher risk of ovarian cysts
Progestagen injections	– Immediate effect – Does not require daily remembering to take the preparation	– Irregular menstruations – Osteopenia, dyslipidaemia – Increase in body weight, androgenic effect
Intrauterine hormonal system	– Comfortable use – Scanty menstruations – Good method for epileptics	– Possibility of falling out, perforation of the uterine wall – Frequent bleeding in the beginning

COC – combined oral contraceptives

- trichomoniasis,
- pediculosis pubis,
- fungal infections (mainly candidiasis),
- HBV and HCV infections,
- gonorrhoea,
- HIV infection,
- syphilis,
- molluscum contagiosum [9-15].

The presence of non-typical symptoms accompanying the above-mentioned infections hinders diagnosis of the diseases, delays their treatment and leads to transmission of the infection to other persons.

Hence, knowledge of the symptoms that may indicate a given disease is extremely important. These include the following:

- pruritus, burning sensation and tenderness of the vagina and vulva in women and of the penis in men,
- pain during sexual intercourse,
- vaginal discharge or urethrorrhoea,
- painful urination,
- eruptions on genitals, around the anus or mouth,
- bleeding during intercourse [16, 17].

The best method that protects against sexually transmitted infections is having a regular partner, and also using a new condom every time before sexual intercourse. It should be borne in mind that condoms do not give 100% certainty of their prevention of all diseases. However, it is not immaterial that a woman is more susceptible to infections, which results from a greater surface area of contact with potentially infectious material in a woman than in a man. In women the area covers the surface of the mucous membrane of the vagina and cervix, while in men it covers only the area of the urethral meatus.

Susceptibility to infections of the reproductive tract is considered to depend on the race and lifestyle of the examined persons. It turns out that persons of non-Caucasian race are more at risk [5, 14], which is associated with the culture and socioeconomic status of these persons. Additionally, in many countries polygamy is common and accepted. This type of relationship is typical of most African countries and the Middle East countries, and specifically people of the Black and Yellow race are definitely more at risk. There are many reasons for this fact, such as low socioeconomic status, low education and poorly developed health care in African countries. Regardless of race, nationality or place of residence, people who have many sexual partners, abuse alcohol, drug addicts, smokers, people of low educational level, with poor personal hygiene, or who suffer from nutrient deficiencies are at increased risk [9-12, 19-21].

Hormonal contraception and sexually transmitted infections

The use of hormonal contraception significantly influences susceptibility to sexually transmitted infections.

There are many reasons for this phenomenon. Unquestionably, the increased level of sexual hormones in the woman's organism, and also her lifestyle and type of the used contraceptives, are of great importance. Many epidemiological and clinical studies have been conducted in order to determine the direct and indirect influence of hormonal contraception on infections [9-15].

Hormonal contraception and bacterial infections

The results of published research on the association between the use of hormonal contraception and bacterial infections are ambiguous.

Some authors state that women who use combined hormonal contraception are less at risk of bacterial infections of the reproductive tract in comparison with women who do not use this method [10, 22, 23]. They also have vaginal gonorrhoeal infections after a sexual contact less often [18]. Thus, modern hormonal contraception could have a protective effect against vaginal bacterial infections [10, 22, 23]. However, some other researchers did not observe such an effect [9, 20, 21], and even found an inverse relationship [9, 13, 19]. Therefore, the issue requires further investigation.

On the other hand, some other studies showed no cytological or bacteriological changes in the cervical-vaginal epithelium in women who used a vaginal contraceptive ring (VCR) containing both oestrogens and progestagens for 20 menstrual cycles [26]. Nevertheless, longer prospective studies are required.

In contrast to COC and VCR, intramuscular progestagen injections increase the risk of bacterial infections of the genital tract, including chlamydial and gonococcal infections [9, 13, 25].

It seems that the risk of infections is strictly correlated with the composition of contraceptives. The combination of oestrogen and progestagen hormones has a greater protective effect in comparison with preparations containing only progestagens. Nevertheless, it should be remembered that also many other factors affect the above relationships. Increased risk of bacterial infections of the genital tract occurs in the following groups [9, 10, 19]:

- prostitutes,
- women who have more than 3 sexual partners per week,
- smokers,
- HIV-1 or HSV-seropositive women,
- women not in formal matrimony,
- black women or women who have black partners.

Also psychological and non-psychological factors may affect the vaginal bacterial flora. It was proved that the highest percentage of Gram-negative bacteria, particularly *Escherichia coli*, was observed in girls before puberty, while the highest occurrence of Gram-positive bacteria was observed in perimenopausal women [23].

More frequent chlamydial infections occur also in women with tubal obliteration. Neither hormonal contraception nor use of condoms increases the incidence of the disorder; nevertheless, using intrauterine devices may lead to tubal obliteration [27]. Pelvic inflammatory disease is less prevalent in women using oral hormonal contraception than in women using an intrauterine device or women not using any of these methods [28]. The effect of mucus thickening is also not immaterial – it prevents the penetration of not only spermatozoa, but also bacteria. It is believed that it is the protective effect against inflammation of the mucous membrane of the uterus, ovaries and Fallopian tubes. It is highly relevant that there is an increased level of interferon γ (IFN- γ), interleukine 10 and 12 (IL-10, IL-12; not IL-4) (RT-PCR) associated with current chlamydial infection, contraceptive pill use and recent sexual intercourse in women aged 13-21 with existing HPV infection [29].

Hormonal contraception and fungal and protozoal infections

Some studies have demonstrated that the risk of *Trichomonas vaginalis* infection is lower in case of using hormonal methods than in using a contraceptive intrauterine device or using none of these methods [14, 30]. In the last two cases the risk of infection is similar [14].

In contrast to protozoal infections, the risk of fungal infections is elevated in case of using hormonal contraceptive therapy [14, 31, 32]. It should be borne in mind that an increased incidence of candidiasis also occurs in antibiotic therapy, impaired immunity (diabetes, alcoholism, immunosuppression, cancers) and in concurrent HIV infection [32].

Hormonal contraception and viral infections

Nowadays, considerable emphasis is placed on the examination of relationships between hormonal contraception and sexually transmitted viral infections, including HIV, HSV and HPV. The results of research on the subject of susceptibility to HIV infections in relation to the used contraception method are ambiguous. This risk is commonly considered elevated [12, 20], but some studies have demonstrated that there is no relationship between increased susceptibility to HIV infections and the use of hormonal contraception by women [33-36]. In addition, no significant differences in the incidence of infections were found between women using COC and those using progestagen injections [33]. What is more, also the use of post-coital contraception (Mifepriston) is not associated with an increased risk of HIV infection [36]. However, the following women are at risk [12, 20]:

- low-educated women,
- women who have many sexual partners,
- women aged 25-35 years,

- women living in cities,
- HSV-seropositive women,
- prostitutes.

Once again it turns out that lifestyle is a very significant factor that determines the potential risk of HIV infection. The results of research conducted on animals are interesting and worth noting – they proved that in contrast to gestagen contraceptives, preparations with oestrogens and gestagens exhibit a protective effect against infections with simian immunodeficiency virus (SIV) [37]. Contraception for HIV-positive women or with AIDS should include a combination of the barrier method and another form of contraception. Oral contraceptives may increase cervical and vaginal shedding of HIV. Some studies have shown that nevirapine and ritonavir may lead to reduced contraceptive efficacy when administered in a combination with oral contraceptives [44].

At present, infection with human papilloma virus (HPV) is one of the most dangerous sexually transmitted infections. In this case, the risk of HPV infection in women using hormonal contraception is increased in comparison with women not using this method of pregnancy prevention [11, 18, 38]. What is more, there is evidence that the risk of cervical cancer is higher in HPV-seropositive women using hormonal contraception [21]. Persistent cervical infections with HPV types 16, 18, 33 may be associated with hormonal contraception – the content of oestrogen and progesterone enhances HPV transcription [1]. Nevertheless, the difference in the incidence of HPV in women using hormonal contraceptives and those using an intrauterine device (without hormones) is not noticeable [38]. Hence, much research is needed in order to determine the direct influence of hormones on the risk of HPV infection, and some other reasons for the increased incidence of HPV infections in women using hormonal contraception should be searched for. Women who are especially at risk include the following groups [11, 18, 21]:

- women with high sexual activity,
- women who have many partners,
- women who became sexually active at an early age,
- smokers,
- women with poor personal hygiene,
- women with nutrient deficiencies,
- women of other race than Caucasian.

A very important aspect that determines the above strong correlation is the fact that women who use hormonal contraception use condoms less frequently than women not using the method, which increases the risk of sexually transmitted infections (Table 3) [2].

Another example of a sexually transmitted viral infection that is associated with the use of hormonal contraception is infection with herpes simplex virus (HSV). It was observed that hormonal contraception increases the incidence of the virus in women's cervical secretions [3, 15, 40]. In addition, preparations containing only progestagens (such as DMPA) may result in an increased risk

Table 3. Duration of contraception use and risk of cervical cancer [39]

Duration of contraception use [years]	Relative risk for all women	Relative risk for HPV-positive women
< 5	1.1	0.9
5-9	1.6	1.3
≥ 10	2.2	2.5

of reactivation of the infection from the latent form by suppressing the protective effect of CD8(+) T cells and by the effect on infected neurons [3]. Other factors that may cause an elevated risk of HSV infection are bacterial vaginal infections, such as vaginal colonization with group B *Streptococcus* [40].

Summary and prevention of infections

As already mentioned, the best contraception method that protects against sexually transmitted infections is using condoms every single time. However, in the whole world women who use hormonal contraception less often demand that their partners use condoms, and only women in whom a sexually transmitted infection was previously diagnosed use condoms more frequently [4]. Thus a vicious circle is developed. Women choose hormonal contraception because of its high effectiveness of pregnancy prevention and come off other mechanical methods, such as condoms. Therefore, the susceptibility to sexually transmitted infections is increased. Despite all these relationships, many women decide to start using hormonal contraception. Nevertheless, the results of studies that proved a reduced risk of bacterial and protozoal infections are comforting [10, 14, 22, 23, 30]. Education of women about protection against infections and prompt treatment in case of infection is very important. Women who have many partners should demand that they use condoms, and also should know the basic symptoms of a current disease of the genital organs in a partner, to be able to consciously decide against sexual contacts or properly protect themselves. Medical and diagnostic examinations are also relevant. Both during the use of hormonal contraception and after discontinuation of using it, regular gynaecological follow-up examinations with cytological examination (sometimes supplemented with molecular and bacteriological examinations), transvaginal USG and breast examination are indicated. Nevertheless, it should be borne in mind that many infections are asymptomatic, and persons unaware of being infected may transmit the infection to their partners. Thus undergoing periodic bacteriological examination may be helpful in diagnosing an asymptomatic infection of the genital tract and beginning appropriate treatment. In case of infection, also a partner of the infected person should be examined. A vaccine

against human papilloma virus (HPV), responsible for cervical cancer, introduced to the market a few years ago, has gained much interest among young girls. Research demonstrated 100% effectiveness of the vaccine in the prevention of chronic HPV infection, precancerous lesions (type CIN2/3) and precancerous vulvar and vaginal lesions [41, 42]. Undeniably, it is a great discovery.

The vaccine has aroused considerable interest worldwide. In a few countries it is reimbursed from state budgets. In other countries, the high cost of the vaccine remains a problem [43].

The choice of hormonal contraception in the light of sexually transmitted infections

Each contraception should be effective and completely safe. Hormonal contraception, despite having the best protection against unwanted pregnancy, offers less protection against sexually transmitted infections than using condoms. Hormonal contraception increases the risk of acquiring sexually transmitted infections indirectly (greater number of sexual partners, early sexual initiation, change in customs – sexual behaviours). On the other hand, many studies have proved that the use of combined oral contraceptives reduces the risk of some sexually transmitted bacterial and protozoal infections. Due to too little unambiguous information about this relationship, one cannot unequivocally state that hormonal contraception acts protectively on the woman's organism against sexually transmitted bacterial infections. It should be remembered that each decision about the beginning of hormonal contraception use ought to be carefully analysed and adapted to the needs and current health status of a patient. Progestagen contraceptives definitely less frequently exhibit the protective effect in comparison with oestrogen-progestagen contraceptives, and sometimes even increase the risk of infection when compared to the control group. Oestrogen is of great importance in the early stage of many infections – it stimulates antibodies and immune response cells. The increase in cytokine expression in peripheral blood and cervical mucus occurs not only in the follicular phase of a woman's menstrual cycle, but also during the use of hormonal contraception [1, 5, 6]. These relationships definitely should be taken into account in the choice of a contraceptive for a patient. Preparations that contain both oestrogens and progestagens (COC, VCR and contraceptive patches) should be recommended to women who are particularly at risk of sexually transmitted infections, while contraceptives with progestagens only (mini-pills, DMPA, IUD) should be avoided. Nevertheless, despite the fact that women who use combined oral contraceptives are less at risk of bacterial infections than women who do not use pills [7, 8, 10, 22, 23], the contraceptives should not be recommended to patients at risk of infections for this reason alone. It is the contraceptives' advantage and not

a sufficient reason for using them. Since millions of women worldwide use hormonal contraception, much research is required to specify accurate recommendations concerning the choice of a proper method of pregnancy prevention in the aspect of sexually transmitted diseases [7, 8, 44].

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