

Review article/Pregledni prispevek

RISKS AND BENEFITS OF ORAL HORMONAL CONTRACEPTION

TVEGANJA IN KORISTI ORALNE HORMONSKE KONTRACENCIJE

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Abstract

Background

Oral hormonal contraception (OC) or the birth control pill that has been in use since 1960 is considered an efficient and reliable method of pregnancy prevention. In the early days the pill contained high doses of hormones, and the related complications were frequently reported. The composition of the pill has substantially changed, estrogen dose has been significantly decreased and so has the incidence of side effects.

Despite the reduced estrogen dose, the risk for the development of vein thromboembolism has not significantly decreased, as the final effect depends on the interaction with the progestagen component. The OC use is in itself an independent risk factor for the development of ischemic stroke event (RR = 1.5), and for the development of myocardial infarction (RR = 1.84). Recent studies show that second generation OC users were at a higher risk of cardiovascular disease than the third generation OC users. The risk of breast cancer is also marginally increased (RR = 1.09-fold increased risk). The discussion about an association between the development of cervical cancer and an increased incidence of the disease in OC users is inclined to attribute this increased incidence to human papilloma virus infection rather than to OC use. Beneficial effects of OC use are manifested through decreased incidence of endometrial cancer, which is mostly true in women with a lower body mass index (BMI). Additionally, OC plays a protective role in the development of ovarian cancer; recent studies have reported that OC use has prevented 200 000 ovarian cancers and 100 000 deaths from the disease. Also, the risk of colorectal cancer in OC users is lower (RR = 0.72).

Conclusions

Modern third generation OC preparations containing desogestrel and gestodene are a safe contraceptive method for all women except for those at increased risk of vein thrombosis.

Key words

oral hormonal contraception; risks; benefits

Izvleček

Izhodišča

Oralna hormonska kontracepcija (OHKC) je v uporabi že od leta 1960 in velja kot učinkovito in zanesljivo sredstvo za preprečevanje nosečnosti. V zgodnji fazi so se uporabljali preparati, ki so vsebovali velike odmerke hormonov, zato je bilo tudi veliko poročil o zapletih. Od začetne faze pa do danes se je sestava kontracepcijske tablete bistveno spremenila, saj vsebuje pomembno manjše koncentracije estrogena, s tem pa so zmanjšani tudi stranski učinki.

Tveganje za razvoj venskih tromboembolizmov se kljub znižanju odmerka estrogena ni bistveno zmanjšalo, ker je končni učinek odvisen od interakcije s progestagensko komponento. Uporaba OHKC je neodvisen dejavnik tveganja za nastanek ishemične oblike možganske kapi z relativnim tveganjem 1,5 in za nastanek miokardnega infarkta z relativnim tveganjem 1,8. Novejše raziskave kažejo, da je tveganje za srčno-žilno obolenje pri uporabi OHKC tretje generacije manjše kot pri uporabi OHKC druge generacije. Mejno se poveča tudi tveganje za nastanek karcinoma dojke (relativno tveganje 1,09). Razprave v zvezi s karcinomom materničnega vratu in uporabo OHKC pa nakazujejo, da je bolj kot OHKC za večjo incidenco te bolezni pri uporabnicah odgovorna okužba s humanim papiloma virusom.

Koristni učinki OHKC se kažejo pri zmanjšanju incidence raka endometrija, kar zlasti velja za ženske, ki imajo nižji indeks telesne mase. OHKC ima tudi protektivno vlogo pri nastanku

raka jajčnikov, saj poročajo, da je uporaba OHKC preprečila nastanek 200.000 primerov raka jajčnika in 100.000 smrti zaradi te bolezni. Tudi tveganje za razvoj kolorektalnega raka je pri uporabnicah OHKC manjše (relativno tveganje 0,72).

Zaključek *Novejši preparati OHKC, ki vsebujejo desogestrel in gestodene, kot tretja generacija oralnih kontraceptivov predstavljajo varno kontracepcijo za vse ženske, razen za tiste, ki imajo povečano tveganje za nastanek venske tromboze.*

Ključne besede *oralna hormonska kontracepcija; tveganja; koristi*

Introduction

Since it was first introduced in the 1960s, the birth control pill has been a popular and extremely effective form of contraception. The oral contraceptive pill is easy to use and when taken correctly, it is 99.9 % successful at preventing pregnancy. Its use, however, has been associated with a number of worrisome side effects. Early research indicated that women taking the pill risked increased rates of heart disease, blood clots and stroke.

Luckily, the picture has improved greatly since those early days. Drug companies have developed new low-dose birth control pills that contain lower levels of estrogen and decrease the risks of unwanted side effects.

Furthermore, not only have the risks decreased, but extensive research over the past twenty years has also shown that there are many real benefits to using the pill that reach beyond contraception.

Risks of oral contraceptive pill

Venous thromboembolism

High dose estrogen preparations are associated with an increased risk of venous thromboembolism. It was previously thought that using low-dose preparations would substantially reduce the risks, but it has become apparent that the effect is also dependent on a complex interaction with the progestagen component. The second generation oral contraceptive pill use, compared with no use, shows a relative risk of 3, whereas the third generation preparations demonstrate a relative risk of 4.8.

The incidence of venous thromboembolism in the general population is 5/100 000/year. The incidence in the second generation OC pill users is 15 cases per year, and in the third generation OC pill users 25 cases per year. To put this risk into perspective, 60 cases of venous thromboembolism per 100 000 occur in pregnancy each year.¹

Cerebrovascular events

Ischemic stroke occurs in 5/100 000 women/year in the population who are usually prescribed the pill. The use of OC pill is an independent risk factor for ischemic stroke by the factor of 1.5. In patients with associated hypertension, the risks of stroke is doubled, and for patients who also smoke the risk is comparatively trebled.

The additional risk is apparent in the first six to 18 months but returns to normal after cessation, with no apparent benefit between the second and the third generation preparations. Patients who carry the Factor V Leiden mutation have a 13-times greater risk of ischemic stroke if on the contraceptive pill, while homocysteinuria patients have a nine-fold increase. The appears to be no increased risk of hemorrhagic stroke in patients under the age of 35 years without additional risk factors.²

Cardiovascular disease

Many studies have attempted to attribute oral contraceptive use as a direct cause of increased risk of myocardial infarction, with RR = 1.84. Several recent studies have shown that in patients younger than 35 years with an uncomplicated medical history and no additional risk factors (hypertension, smoking or obesity) there is no significant additional risk. But in women older than 35 there appears to be a two to three fold increase in the incidence of cardiovascular events amongst those who take combined oral contraception.

Several studies have looked at looked at the role of different formulations of progesterone and their cardiovascular effect. Although there is no conclusive evidence, it has been suggested that there may be a reduced cardiovascular risk associated with the third generation preparations over the second generation pills.³

Breast cancer

A large cohort studies have shown that women who have used the OC pill are associated with a marginally increased risk of breast cancer (RR = 1.09). No strong associations in relation to age started, durations of use, time since the first or last use or use related to pregnancy have been observed. This associated risk of developing breast cancer returns to the same level as in women who have never used the pill within ten years of the last use.

Cervical cancer

The International Agency for Research on Cancer classifies the OC pill as a cause of cervical cancer. Yet, there has long been a debate as to whether there is a direct causal association between the pill and the disease or an indirect effect relating to changes in sexual behaviour leading to an increase in exposure to carcinogens, primarily the human papillomavirus.⁴

Benefits of combined oral contraception

Endometrial cancer

Several epidemiologic studies have observed a protective effect from endometrial cancer conferred by use of the oral contraceptive pill, with the benefit persisting for more than 25 years. The majority of current OC preparations are potent enough to have a beneficial influence, but it has been found that women with a lower Body Mass Index (BMI) receive a greater protective effect than those with a higher BMI on formulations containing a low dose of progesterone.⁵

Ovarian cancer

The association between the protective effect of the OC pill and ovarian cancer has long been established. A recent large study suggests that in high-income countries, ten years' use of the oral contraceptive pill is estimated to reduce the incidence of ovarian cancer ($p < 0.0001$) before the age of 75 from 1.2 to 0.8 per 100 users, with a reduction in mortality from 0.7 to 0.5 per 100 users.

The protective effect of the pill becomes apparent after a short latency period and increases with duration of use, with each year of use conferring an estimated 5 % reduction in risk.

The proportional risk reduction for ovarian epithelial cancers with OC pill use is 29 % for individuals who stopped using the pill less than ten years ago; 19 % for those who stopped between 10 and 19 years previously, and 15 % for those who stopped 20 and 29 years previously.^{6,7}

A recent report suggests that oral contraceptive use has already prevented 200 000 ovarian cancers and 100 000 deaths from the disease. Over the next few decades, the number of cancers prevented is expected to rise to at least 30 000 cases per year worldwide.

Colorectal cancer

Following the publication of several studies regarding hormone replacement therapy, a considerable interest has evolved regarding the role of exogenous hormo-

nes and bowel carcinogenesis. The use of the OC pill has been associated with a modest risk reduction of developing colorectal cancer (RR = 0.72), with a consistent effect on all tumor subsites within the rectum. However, no apparent correlation between the duration of use and benefits has been observed.

Other non-contraceptive benefits of oral contraceptives include reduction in menstrual-related or perimenopausal symptoms, improvement of acne, fewer ectopic pregnancies, maintenance of bone mineral density, and a possible protection against pelvic inflammatory disease.⁸

Conclusion

Although the third generation oral contraceptives (containing desogestrel and gestodene) most likely increase a user's risk of venous thromboembolism, their improved side-effect profile and their possible decreased association with myocardial infarction and stroke may make them a useful new class of oral contraceptives for most women except those at increased risk of venous thrombosis.

References

1. Burkman RT. Oral contraceptive: Current Status. In: Archer DF (ed.) Contraception for the 21st century. Clin Obstet Gynecol 2001; 44: 62-72.
2. Steinberg WM. Oral contraceptive user compliance: How to improve it. Gynecol Endocrinol 1995; 9(Suppl. 1): 1-4.
3. WHO Working Group. Cardiovascular Disease and Steroid Hormone Contraception. Geneva: World Health Organization, 1998.
4. Ursin G, Peters RK, Henderson BE, Abalaing G, Monroe KR, Pike MC. Oral contraceptive use and adenocarcinoma of cervix. Lancet 1994; 344: 1390-4.
5. Gambrell RD. The role of hormones in etiology and prevention of endometrial cancer. Clin Obstet Gynaecol 1986; 13: 695-723.
6. Sperof L, Darney PD. A Clinical Guide for Contraception. 3rd Edition. Philadelphia, USA: Lippincott, Williams and Wilkins, 2001.
7. Walker GR, Schlesselman JJ, Ness RB. Family history of cancer, oral contraceptive use and ovarian cancer risk: Am J Obstet Gynecol 2002; 186: 8-14.
8. Coker AL, Harkap S, Formey JA. Oral contraceptives and reproductive cancers: Weighing the risk and benefits. Fam pPlann Perspect 1993; 25: 17-21.