CPD Paper 8

The Combined Oral Contraceptive Pill in Women Over Age Forty

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Abstract

Introduction**: By the age of 35 years, most women would have completed their families and contraception then becomes an important consideration. In the next one or two decades, other health concerns such as osteoporosis, dysfunctional uterine bleeding, ovarian, endometrial, colorectal and breast cancers and cardiovascular diseases will assume prominence in the lives of women. We review the role of the combined oral contraceptive (OC) pill in the older woman in the context of these important health concerns. **Methods**: A Medline search was made for possible interaction between OC use and the above conditions. An important criteria for citation was publication in a high impact factor journal; furthermore to represent the wider context from which there issues derive we choose, whenever appropriate, general journal with wide readership including, but not limited to the* **Lancet** *or* **New England Journal of Medicine; we also choose studies published in journals of other medical disciplines instead of purely gynaecological journals to reflect the multidisciplinary impact of the combined OC pills. **Results**: Combined OC retards bone demineralisation which could translate clinically to a reduction in postmenopausal osteoporotic fractures; it affords good menstrual cyclicity and alleviation of perimenopausal vasomotor symptoms; it offers chemoprophylaxis against epithelial ovarian cancers and endometrial cancers. There is evidence that it could be protective against colorectal cancers. The combined OC may attenuate the disease progression of rheumatoid arthritis and reduces the risk of ectopic pregnancy and pelvic inflammatory disease. In an older woman who does not smoke and is in good health, the excess risk of stroke, myocardial infarcts and venous thromboembolism is minimal, if at all, as is the risk of breast neoplasm. In women with proven human papilomavirus infection of the cervix who are using OCs, regular cervical screening is especially important. **Conclusion**: The non-contraceptive health benefits of the combined OCs justify its usage in the healthy older woman.*

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Introduction

In the 1970s, several studies appeared to suggest that users of oral contraceptives (OCs) were at increased risk of cardiovascular events. More recently following newer studies on lower dose OCs and re-analysis of the old studies, it was concluded that the risk of cardiovascular accidents was attributable primarily to smoking; when smokers were excluded from the final analysis, OCs did not result in an excess risk of strokes, myocardial infarcts (MI) or thrombo-embolic events for users at any given age. Despite this finding, physicians and patients were reluctant to use OCs in women beyond 35 years of age, preferring alternative methods of contraception. Women aged 40-44 years are still relatively fertile and require reliable contraception if pregnancy is to be avoided; women aged 45-52 years commonly experience dysfunctional uterine bleeding. The present authors advocate OCs as ideal for women in their 40s, both in terms of being an effective contraception and possessing numerous non-contraceptive benefits, which include menstrual regulation, amelioration of vasomotor symptoms, preservation of bone mineral density, reduction in the risk of postmenopausal osteoporotic fractures, decreased incidence of ovarian, endometrial and colorectal cancers. OCs also decrease risk of ectopic pregnancy and pelvic inflammatory disease and may attenuate the severity of rheumatoid arthritis. Moreover, latest research showed that OC use, even for a long period, is not associated with an increased risk of breast cancer. Regular cervical screening should be performed for all women on OCs especially in those who are positive for human papillomavirus infection of the cervix. Therefore, the challenge lies in physician and patient education regarding the risks and advantages of OCs in women above 40 years of age.

The perimenopause is defined as a transition period between the age of 45 years and 1 year after menopause. Due to the gradual cessation of ovarian function and the wide fluctuations of the hormonal environment, patients in their mid 40s will begin to experience manifestations of this transition. These problems include disturbances in menstrual

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cycle, vasomotor symptoms and loss of bone mineral density. Although the cycle length begins to shorten, the potential for ovulation and pregnancy is preserved for a number of years. Therefore, the contraceptive needs of this cohort of women must not be neglected. It is also timely that physicians focus on the unique health issues of this group of women, tide them through the perimenopause and help make their transition into the menopause smoother. Tessler and Peipert,[1] in a survey of educated women, found that even amongst the better educated, knowledge about the non-contraceptive benefits of OCs was deficient: only 5% were aware that OCs protected against benign breast cyst; 9% knew it protected against ectopic pregnancy; 10% knew it protected against pelvic inflammatory disease; 19% and 23% knew it attenuated the risk of endometrial cancer and ovarian cancer, respectively. All suspected OCs induced breast cancer or they were detrimental to health. In one study,[2] the percentage of women aged 35 to 39 years who used OCs was 21%, declining to 11% in those aged 40 to 44 years and further falling to 4% in women aged 45 to 50 years. This may reflect physicians' and patients' misconception about the safety profile of OCs leading to this declining trend in prescription as age advances. We need a better understanding of hormonal contraception in order to advocate its use judiciously and effectively. This paper aims to show the benefits of providing a hormonal continuum bridging the reproductive era and the postmenopausal years.

Contraception

Many perimenopausal women fail to appreciate the continuing need for effective contraception. Women between the ages of 40 and 44 years can still conceive. The National Survey of Family Growth also showed that 51% of pregnancies that occurred in women aged 40 and older were unintended and 65% of these culminated in abortion.[3] If OCs are used as recommended, the chance of becoming pregnant during the first year is 0.1%. However, typical pregnancy rates are estimated to be 5%. The effective contraception provided by OC use offers perimenopausal women the same protection against pregnancy that is afforded to younger women. Fortunately, OC use is safe in healthy non-smoking women until menopause.

Non-Contraceptive Health Benefits

Osteoporosis

There is a large body of evidence to suggest that OCs have a beneficial effect on bone mineral density (BMD). Gambacciani et al[4,5] evaluated the effects of 20 mg ethinylestradiol (EE) and 0.15 mg desogestrel on bone metabolism and bone mineral density in perimenopausal women. They found that, in OC-treated women, osteocalcin plasma levels and urinary excretion of hydroxyproline significantly decreased leading to a significant increase in vertebral and femoral bone density. Volpe et al[6] showed that, in women with normal cycle, the administration of OCs did not increase bone mineral denisty; in women with perturbances in menstrual cyclicity, bone turnover was increased and bone mineral density reduced. In this group of women, administering OCs retarded bone loss and restored bone mineral density. Volpe et al concluded that OCs are indicated to prevent postmenopausal osteoporosis in perimenopausal women with ovulatory disturbances.

De Cherney[7] showed that the positive association between OC use and bone mineral density was directly related to the duration of OC use and with the optimal dose of ethinyl estradiol of 25 mg to 35 mg. Corson[8] showed that long-term perimenopausal OC exposure allowed women to enter menopause with a BMD that was 2% to 3% higher than non-users. Lindsay et al[9] found that vertebral BMD increased by about 1% for each year of OC exposure.

A recent meta-analysis of 13 studies by Kuohung et al[10] to determine the association between OC and BMD was carried out. Nine of the studies found a positive effect of OC on BMD. Four studies failed to show such a link. None, however, showed a decrease in BMD with OC use. They concluded that OC generally had a favourable effect on BMD.

Michaelsson et al,[11] in their case-control study, showed that premenopausal women who took OCs decreased their risk of postmenopausal osteoporotic fractures by 25% and women who used a 50-mg ethinyl estradiol pill had a 44% lower risk of hip fracture. In this study, compared to women who had never used OCs, the odds ratios (ORs) for hip-fracture were 0.69 [95% confidence interval (CI) 0.51-0.94], for use after the age of 40 years; 0.82 (95% CI, 0.57-1.16), for use between 30 and 39 years of age; and 1.26 (95% CI, 0.76-2.09), for use below 30 years of age.

With the recent controversies surrounding the use of hormone replacement therapy (HRT) following the Women's Health Initiative (WHI) report,[12] there may be a role for OC use until menopause in selected patients at risk of osteoporosis.

Menstrual Regulation

The decline in ovarian reserve in the perimenopausal woman results in anovulation, which manifests itself in a variety of forms of menstrual cycle disturbances. This dysfunctional uterine bleeding (DUB) not only is annoying for women but also can put them at increased risk for endometrial hyperlasia.

For decades OCs have been used to control uterine bleeding and regularise menses. Now, there are data showing that use of a specific OC formulation regularises menses in women complaining of DUB.[13] In a double-blind, placebo-

controlled, multicentre trial, 201 women with menorrhagia, meno-metrorrhagic, oligomenorrhoeic or polymenorrhoeic dysfunctional uterine bleeding were randomised to receive a triphasic OC (norgestimate ethinyl estradiol) or placebo for 3 cycles. Results of the trial demonstrated that significantly fewer women receiving OCs than those receiving placebo reported abnormal bleeding. For each subtype of dysfunctional uterine bleeding, improvement was noted for subjects in the OC group. In addition, improvement in physical function (e.g., self-care, walking, lifting, bending, exercise) was greater with the OC than with placebo.

Gynaecological Cancers

Several studies have shown the use of OCs reduces the risk of both ovarian and endometrial cancers. In the Cancer and Steroid Hormone Study (CASH),[14,15] there was a 40% reduction in the risk of ovarian cancer after as short a period as 3 to 6 months of use, and 10 or more years of use was associated with a 80% reduction in the risk. Furthermore, there was a 40% reduction in the risk of endometrial cancer after 12 months of OC use. For both ovarian and endometrial cancers, the protection conferred was still evident 15 years after last OC use. However, carriers of the BRCA1 or BRCA2 mutation have not been shown to benefit from OC use in terms of reduction in risk of ovarian cancer.[16]

Vasomotor Symptoms

There is evidence showing OCs relieve vasomotor symptoms in perimenopausal women.[17] In a 3-year, prospective cohort study comparing 100 perimenopausal women treated with a triphasic OC (ethinyl estradiol 30/40/30 mg and levonorgestrel 0.05/0.075/0.125 mg) with a similar number of age-matched untreated group, 90% of the OC users obtained complete relief of vasomotor symptoms after 2 months' use, and the remaining 10% responded after 3 months. In contrast, 60% of untreated women had no improvement in vasomotor symptoms during these 3-month observations.

Other Long-term Health Benefits of OC Use

Protection against colorectal cancer: OC appears to be protective against colorectal cancers.[18] A pooled estimate from 8 case-control studies and 4 cohort studies found the OR to be 0.82 (95% CI, 0.74-0.92).

Reduced occurrence of rheumatoid arthritis: In a recent prospective study, women with rheumatoid arthritis and who were on long-term OC use had less radiographic joint damage and better functional level.[19] This seems to corroborate earlier studies that OC may prevent the progression to severe disease by modifying the disease process.[20]

Decreased risk of ectopic pregnancy: OCs also lower the risk of ectopic pregnancy: Franks et al[21] found a 500-fold decrease in rate of ectopic pregnancy between OC users and non-contraceptive users.

Decreased risk of pelvic inflammatory disease-related hospitalisation: Panser and Phipps[22] found a potentially protective effect of OCs against pelvic inflammatory disease that required hospitalisation, whilst another study[23] indicated that OC use protected against symptomatic pelvic inflammatory disease in women infected with *Chlamydia trachomatis* but not *Neiserria gonorrhoea*.

OC Risks

Many studies emanating from the 1970s and 1980s reported an association between OC use and adverse events, such as thromboembolic phenomena, cerebral and MI. Numerous recent studies have unequivocally pointed out that the adverse outcomes were related to the higher dose oestrogen content in the older OC preparations. To put the risk of OC use in perspective:[24] the overall risk of death from cardiovascular disease of women between 35 and 44 years of age who neither smoked nor used OCs was 5.2 per 100,000 woman years. The risk of death from a term pregnancy in women of the same age category was 16 per 100,000 woman years. In contrast, the risk of death in women between 35 and 44 years of age who used OCs but were non-smokers was 6.2 per 100,000 woman years. The attributable risk of death from OC use in women in this age group was estimated as 3.03 per 100,000 user years. However, the cardiovascular mortality risk in women above 35 years old who used OCs and smoked was 29 per 100,000 woman years and the risk attributable to OC use was 19 per 100,000 user years. The risk of dying from a motor vehicle accident was 12.8 per 100,000 woman years.[24]

Venous Thromboembolism (VTE)

Women who use OCs have a risk of VTE, about 3-fold higher than those who do not.[25] Notwithstanding this increase, the absolute risk is very small. Comparatively, the risk of VTE in pregnancy is 5-fold that of a non-pregnant woman of the same age.[26] The incidence of pregnancy-related VTE has been quoted as 6 per 10,000.[27]

Both the World Health Organization (WHO)[28] and Transnational Studies[29] consistently showed that third-generation OCs increased the risk of VTE compared to second-generation OCs. Adjusted ORs were 1.5 (95% CI, 1.1-2.1) for the Transnational Study and 2.7 (95% CI, 1.6-4.6) in the WHO study. Jick et al[30] showed that the relative risk of VTE with desogestrel was 1.9 (95% CI, 1.1-3.2) and 1.8 (95% CI, 1.0-3.2) with gestodene compared to levonorgestrel. The excess risk for non-fatal VTE with the new generation OCs with low-dose oestrogen and either

desogestrel or gestodene was 16/100,000 woman years compared to levonorgestrel.

However, a nested case control British study evaluating the association between VTE and different formulations found no difference in the risk between second- and third-generation OCs.[31] A recent review by Kaper et al[32] concluded that both second- and third-generation OCs carry similar risks for venous thrombosis.

A re-analysis of the Transnational Study by Suissa et al[33] found that, for first-time users, the adjusted rate ratio of VTE as a function of the duration of OC use was essentially identical for second- and third-generation OCs relative to never users. This rate ratio increased to around 10 in the first year of use and decreased to around 2 after 2 years of use and stabilised at this rate thereafter for both second- and third-generation OCs.

Yet in a meta-analysis by Kemmeren et al,[34] a 1.7-fold increase in the risk of VTE was found amongst users of third-generation OCs compared to second-generation OCs.

When the pattern of OC use[35] was evaluated, it showed that the adjusted rate ratio of VTE for repeat users of third-generation OCs was 0.6 (95% CI, 0.3-1.2) relative to repeat users of second-generation OCs. The adjusted rate ratio was 1.3 (95% CI, 0.7-2.4) for patients who switched from second to third-generation OCs relative to those who switched from third- to second-generation OCs. The authors concluded that second- and third-generation OCs were associated with equivalent risks of VTE when the same OC was used repeatedly after interruption, or when users switched between the 2 generations of OCs.

Cerebral Infarcts

A plethora of studies have sought to clarify the relationship between the use of OCs and strokes with conflicting results. In 1996, Petitti et al[36] looked at OC use in women between 15 and 44 years of age and reported no increase in the risk of either ischaemic or haemorrhagic stroke with low-dose OCs. A total of 408 confirmed strokes occurred in 1.1 million women, with a total of 3.6 million woman years of observation. The OR for ischaemic stroke among current users of OCs as compared to former users and women who were never exposed to OCs was 1.18 (95% CI, 0.54-2.59) after adjusting for other risk factors for stroke. For haemorrhagic stroke, the OR was 1.14 (95% CI, 0.60-2.16). But smoking was seen to increase the risk of haemorrhagic stroke in OC users. Similarly, in 1997, Schwartz et al[37] concluded that the overall risk for stroke and type of stroke was not increased among users of low-dose OCs when they evaluated OC users in women aged 18 to 44 years. In this study, there was no demonstrable evidence that the OR for OC use and stroke was elevated because of age, smoking or obesity. Moreover, neither "current use" nor "past use" compared to "never use" increased the risk of either type of stroke or incidence of total strokes.

Schwartz et al,[38] in a pooled analysis of the above 2 studies, concluded that the pooled OR for current low-dose OC use and either stroke type was not elevated in women who were above 35 years, cigarette smokers, obese or non-hypertensive. But amongst women with migraine, the risk for ischaemic stroke was increased. This pooled analysis also found an inverse relationship between past OC use (irrespective of formulation) and ischaemic stroke, but not to haemorrhagic stroke.

Yet other investigators reported different findings. Heinemann et al[39] looked specifically at ischaemic stroke in users of low-dose OCs aged 16 to 44 years and found a small, but significant relative risk. Adjusted ORs for ishaemic stroke were 4.4 (95% CI, 2.0-9.9), for current users of first-generation OCs; 3.4 (95% CI, 2.1-5.5), for second-generation OCs; and 3.9 (95% CI, 2.3-6.6) for third-generation OCs. The risk ratio for third- versus second-generation OCs was 1.1 (95% CI, 0.7-2.0).

In 1996, the WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception in 1996 published 2 papers,[40,41] one pertaining to the association between OC and ischaemic stroke and the other pertaining to haemorrhagic stroke. That was a substantial increase in the relative risk of ischaemic stroke among OC users with a history of hypertension (other than during pregnancy) and among those who smoked. But there was no significant increase in OR with increasing duration of OC use among current users. Upon cessation of OC use, this risk returned to baseline.

Regarding haemorrhagic stroke, the findings showed that in women under 35 years, the use of OCs did not affect the risk of haemorrhagic stroke. But women above 35 years of age, taking low-dose OCs, were at slightly increased risk for haemorrhagic stroke particularly in those from developing countries. OC use and smoking or hypertension drastically increased the risk of haemorrhagic stroke.

Acute Myocardical Infarcts

A WHO multicentre study[42] found that the risk of low-dose OC users developing acute myocardial infarction (AMI) was increased in women with cardiovascular risk factors like smoking and hypertension. No consistent association between the OR for AMI and age of OC users was apparent. No significant increase in OR was apparent with increasing duration of OCs use among current users or in women who had stopped OCs after long exposure. Only among older women who smoked was the degree of excess risk associated with OCs substantial (400 per 1,000,000), but in absolute terms this was small. This study had no

power to evaluate between progestagen types.

Sidney et al,[43] in a population-based case control study, studied women aged 18 to 44 years with incident of MI with no past history of cardiovascular event. Compared with never users, the ORs for MI after adjusting for risk factors were 0.56 (95% CI, 0.21-1.49) in current OC users and 0.54 (95% CI, 0.31-0.95) in past OC users. Among past OC users, duration and recent use were unrelated to risk of MI. In this study, no evidence of interaction between age and OC use and risk of MI was found ($P = 0.28$; OR 1.21; 95% CI, 0.45-3.26) in women under 40 years and OR, 0.40 (95% CI, 0.06-2.67) in those above 40 years of age. Women were also stratified according to whether they had cardiovascular risk factors, such as hypertension, hypercholesterolaemia and diabetes, or according to whether they were obese or smokers. There was no interaction between OC use and any of the above in influencing the risk of MI. There was no difference between norethindrone and norgestrel type progestagen in modifying the risk of MI.

However, Tanis et al[44] found that the risk of MI was increased among women who used any type of OCs compared to non-users (OR 2.9; 95% CI, 1.5-2.8). The adjusted OR was 2.2 (95% CI, 1.5-4.1) amongst women who used second-generation OCs; amongst women who used third-generation OCs the adjusted OR was 1.3 (95% CI, 0.7-2.5). This study also found that the risk of MI was the same whether or not they had a prothrombotic mutation such as Factor V Leiden or a mutation in the prothrombin gene G20210A.

Breast Cancer

The Collaborative Group on Hormonal Factors in Breast Cancer[45] reviewed 90% of the available epidemiological data on the relationship between breast cancer and hormonal contraception involving more than 53,000 women with breast cancer and 100,000 without. Three conclusions were drawn: firstly, in women taking the combined OCs and in the 10 years after stopping, there was a small increase in the relative risk of having breast cancer. In current users, this relative risk was 1.24 (96% CI, 1.15-1.33); 5 to 9 years after stopping OC use, the relative risk was 1.07 (95% CI, 1.02-1.13). However, this is the same risk one can expect with pregnancy. Secondly, there was no significant excess risk of having breast cancer diagnosed 10 or more years after stopping use. Finally, the cancers diagnosed in women who had used combined OCs were less advanced clinically than those diagnosed in women who had never used OCs.

However, a population-based, case-control study, which evaluated women aged 35 to 64 years with exposure to hormonal contraception, found that in 4575 women with breast cancer and 4682 controls, current or former OC use was not associated with a significant increase in risk of breast cancer; the relative risk did not increase with longer periods of use or in women with a family history of breast cancer.[46]

Melanoma

A recent study failed to establish any association between OC use and development of melanoma.[47] Duration of OC use, age at first use, years since first use or last use, or current use did not affect the incidence of melanoma.

OC and Invasive Cervical Cancer

Smith et al,[48] in a recent review, analysed data from 28 studies including more than 12,000 women with cervical cancer with regard to hormonal contraception use and presence of human papillomavirus (HPV). The majority of the hormonal contraceptives were of the combined oestrogen-progestagen formulation. For all women the relative risk of developing cervical cancer increased with duration of OC usage. Compared to never users of OCs, the relative risks of cervical cancer for use less than 5 years, between 5 and 9 years and more than 10 years were 1.1 (95% CI, 1.1-1.2), 1.6 (95% CI, 1.4-1.7) and 2.2 (95% CI, 1.9-2.4), respectively. When the analysis was restricted to women with HPV, the corresponding relative risks were 0.9 (95% CI, 0.7-1.2), 1.3 (95% CI, 1.0-1.9) and 2.5 (95% CI, 1.6-3.9), respectively. When the analysis was performed on women without HPV, the OR of cervical cancer compared to never users was 0.83 (95% CI, 0.54-1.27). For less than 5 years of OC use, the OR of cervical cancer was 0.77 (95% CI, 0.48-1.23); for use between 5 and 9 years, the OR was 0.56 (95% CI, 0.30-1.03); and for use more than 10 years, 1.09 (95% CI, 0.70-1.71). The trend was statistically significant even after adjusting for potentially confounding factors such as number of sexual partners, previous cervical screening, smoking or use of barrier contraception. The results applied for both squamous cell carcinoma and adenocarcinoma. The data also indicated that, for past users (last use more than 8 years ago) whose duration of use was more than 5 years, the relative risk of cancer was 1.4 (95% CI, 1.1-1.9). For current users and recent users (last use less than 8 years ago) whose duration of use exceeded 5 years, the relative risk was 2.1 (95% CI, 1.8-2.4).

In a study by Moreno et al,[49] which was also included in the above meta-analysis, it was shown that age at first use and time since first use of OCs did not significantly affect the relative risk of cervical cancer after adjusting for duration of use. This study also suggests a persistent increased risk of cervical cancer 5 to 14 years after stopping OCs in those who had used it more than 5 years (RR 4.14; 95% CI, 1.55-11.06). This contrasts with another study of 46,000 OC users (average duration of use was 5 years) followed-up for 25 years, which found that among current

and recent users (within 10 years) the relative risk of death from cervical cancer was 2.5 (95% CI, 1.1-6.1). Women who had stopped OC use more than 10 years did not have any excess risk of cervical cancer. The authors concluded that there was no evidence of a persistent effect 10 years after stopping OCs.[50]

Munoz et al[51] proved a positive association existed between parity and risk of squamous cell carcinoma of the cervix among women positive for HPV and this risk was compounded by OC use. The OR of cervical cancer in a woman who used OCs for more than 5 years and had more than 5 full-term pregnancies (FTP) was 11.75 (95% CI, 5.21-26.50). Nulliparous women using OCs for more than 5 years did not have an increased risk of cervical cancer. The OR for women with more than 5 FTP but had never used OCs was 3.35 (95% CI, 2.32-4.85). The results were adjusted for study centre, age, education, smoking, age at first intercourse, number of sexual partners and history of Papanicolaou smears. However, it is not clear in women using OCs and had pregnancies whether the usage was intermittent or continuous or was the duration the total time used.

However, OC use does not appear to increase the risk of HPV infection. In a review of 19 epidemiological studies of genital HPV and OCs, Green et al[52] found no evidence for either a positive or negative association between long duration of OC use and HPV status.

The mechanism of viral carcinogenesis was reviewed recently.[53,54] Sex steroids have been postulated to be one mechanism whereby HPV exerts its tumorigenic effect on the cervix. Steroids such as oestrogen are thought to bind to specific DNA sequences within transcriptional regulatory regions on the HPV DNA to either increase or suppress transcription of various genes. The role of steroid was further established by the discovery of hormone receptors in cervical tissue. The upstream regulatory region (URR) of the HPV type 16 viral genome mediates transcriptional control of the HPV genome and is thought to contain enhancer elements that are activated by 16 alpha hydroxylation by oestrogen. This leads to an increase in E6 and E7 HPV 16 oncogenes which bind to p53 tumour suppressor gene and stimulate their degradation by a ubiquitin-dependent protease system leading to apoptotic failure and carcinogenesis.

In older women who are on the OCs, regular cervical screening is especially important as HPV status is not always known.

In an interesting meta-analysis, Schlesselman[55] found that the net effect of the risks and benefits of OCs on the various types of cancers was probably negligible. For every 100,000 women in the United States who never used OCs, the numbers developing cancer between 20 and 54 years are estimated to be 2782 (breast), 425 (cervix), 438 (endometrium), 369 (ovary) and 20 (liver). For women using OCs for 8 years, the estimated number of additional or fewer cases per 100,000 women were +151 (breast), +125 (cervix), -197 (endometrium), -193 (ovary) and +41 (liver).

Conclusion

Women in their 40s still require contraception. The perimenopause is a phase in a woman's life when declining ovarian function results in menstrual irregularities, vasomotor symptoms and bone loss. OCs are able to resolve many of these problems and may have other benefits, such as reducing the severity of rheumatoid arthritis, continued protection against ovarian and endometrial cancers long after stopping OC use, and reduction in colorectal cancer. In addition, it is a very effective contraceptive. In women who do not have any risk factors for cardiovascular events, the benefits appear to outweigh the risks. Whether OCs actually increase the risk of VTE, strokes or MI requires further research, but even if an association exists, this is likely to be minimal in absolute numbers. The risk of breast cancer appears minimal. Regular cervical screening is especially important for users of OCs especially those with HPV infection of the cervix. Continuing OC use through the perimenopause allows women to enter menopause healthier and with an improved quality of life than her counterparts who do not use OCs. The reluctance of physicians to prescribe and patients to use OCs stems from undue and sometimes unfounded fear of its adverse effects which when seen in proper perspective may be negligible.

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QUESTIONS

1. In perimenopausal women
   a) ovarian reserve is reduced.
   b) ovulatory menstrual cycle disturbances occur.
   c) there is an increased risk of endometrial hyperplasia.
   d) oral contraceptive pills are not an accepted form of managing menstrual disturbances.
   e) contraceptive is still an important concern in these women.

2. The use of oral contraceptive is associated with
   a) reduction in endometrial cancer.
   b) reduction in ovarian cancer.
   c) increase in invasive cervical cancer.
   d) increase in colorectal cancer.
   e) increase in breast cancer.

3. Benefits in oral contraceptive include
   a) reduced occurrence of rheumatoid arthritis.
   b) prevention of Alzheimer's disease.
   c) prevention of irritable bowel syndrome.
   d) decreased risk of ectopic pregnancy.
   e) decreased risk of pelvic inflammatory disease.

4. In oral combined contraceptive users, there
   a) is an increased risk of venous thromboembolism.
   b) the risk of ischaemic stroke is higher.
   c) the risk of haemorrhagic stroke is higher.
   d) the risk of developing acute myocardial infarct is higher.
   e) the risk of hypercholesterolaemia is increased.

5. With regard to oral contraceptives and invasive cancer
   a) the risk of developing cervical cancer decreased with duration of oral contraceptive usage.
   b) age of first use of oral contraceptives was a significant risk factor.
   c) nulliparous women using oral contraceptives were at a greater risk.
   d) oral contraceptive use increases the risk of human papillomavirus infection.
   e) regular cervical screening is important for perimenopausal women on oral contraceptives.