Non-contraceptive effects and uses of hormonal contraception

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Abstract

Most women feel confident taking the modern combined oestrogen-progestogen oral contraceptive pill (COCPs) but myths about these drugs still persist. Most non-contraceptive health benefits of COCPs are not widely appreciated, in spite of much evidence. Controversy still exists over the association between COCP use and breast cancer. Although slightly more breast cancers are detected in current COCP users they are less advanced in stage and less aggressive in behaviour. This article discusses the non-contraceptive benefits and uses of hormonal contraception.

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Introduction

The combined oestrogen-progestogen oral contraceptive pill (COCP) was first marketed for the treatment of menstrual disturbances, in 1957 in the United States.[1] With the increasing popularity of "the pill" for contraception, anecdotal evidence started to accumulate for a range of beneficial health effects and it became widely used (without rigorous supporting evidence) for the treatment of various gynaecological symptoms.[2]

It became clear that the COCP could offer women health benefits in three ways: by providing highly effective contraception, by treating some gynaecological symptoms and by preventing some gynaecological and medical conditions.[3]

Health benefits associated with the use of hormonal contraceptives have not received the same degree of research or publicity as have potential adverse effects, and the quality of evidence for such benefits is highly variable.

Treatment of gynaecological disease

Conditions that may respond to COCP treatment are listed in Table I. Primary dysmenorrhoea is the condition that responds best. While most of the evidence for this effect comes from studies with medium dose (50 µg oestrogen) COCPs,[4] low dose (20 µg oestrogen) COCPs are likely to have a similar effect.[5] The benefit is probably associated primarily with the suppression of ovulation. Secondary dysmenorrhoea due to chronic pelvic inflammatory disease or endometriosis may also respond, albeit to a lesser degree, to COCP treatment. One randomised, open-label study reported that the COCP was as effective as GnRH (Gonadotrophin-Releasing Hormone) in reducing dysmenorrhoea due to endometriosis, but less effective in reducing deep dyspareunia.[6]

In most women COCPs are also able to provide effective control of menstrual cycle symptoms such as menorrhagia (E2), dysmenorrhoea (E1) and premenstrual syndrome (E1).

Evidence that the COCPs alleviate other cyclical symptoms such as mid-cycle pain, perimenstrual migraine, menstruation-related epilepsy and more rare symptoms, is limited. Many of these conditions are so uncommon that randomised trials for treatment are not feasible. The most effective approach to treating these conditions may be the continuous use of COCPs (i.e. with no monthly break) or the use of a progestogen-only method that inhibits ovulation, provided that breakthrough bleeding is not a problem.

Menorrhagia due to ovulatory dysfunctional uterine bleeding usually responds well to COCP treatment, whereas the response of menorrhagia caused by other conditions is quite variable.[7] The best evidence comes from studies with COCPs containing 50 µg oestrogen.[7] It is not clear whether the same level of benefit occurs with the lowest-dose pills currently available,[8] although a randomised, placebo controlled, double blind trial of COCPs delivering either 20 µg or 30 µg of oestrogen, has shown

Table I: Evidence for treating symptoms with COCPs*

Symptom	Approximate proportion of sufferers whose symptoms are reduced by COCPs	NHMRC level of evidence[6]
Menorrhagia		
- Ovulatory dysfunctional uterine bleeding	60% (with 50 µg oestrogen COCPs)	II
- Anovulatory dysfunctional uterine bleeding	Uncertain	IV
- Coagulopathy	Uncertain	IV
- Uterine fibroids	Uncertain	IV
- Iron deficiency anaemia	Uncertain	II
Primary dysmenorrhoea	70% (with 50 µg oestrogen COCPs)	II
Secondary dysmenorrhoea	40%	II
Premenstrual syndrome	< 30%	III
Acne	30% - 80% (depending on formulation)	II
Hirsutism	< 10%	IV
Other cyclical symptoms	Variable	IV

COCP – combined oestrogen-progestogen oral contraceptive pill.
There have been few randomised controlled trials of the effect of COCPs on these disorders. Much of the evidence comes from case-control and cohort studies, often with older and higher-dose preparations (similar studies using modern very low-dose (20 µg) COCPs are rare).
References have not been included for uncommon conditions or weak associations.
NHMRC – National Health and Medical Research Council

that these dosages significantly reduce dysfunctional uterine bleeding.

The use of COCPs tends to raise haemoglobin levels, especially in women with a convincing clinical history of menorrhagia, and reduces the severity of iron deficiency anaemia.[9]

Acne responds well to treatment with COCPs. The mechanism involves partly a decrease in ovarian secretion of testosterone, partly an increase in the production of sex-hormone-binding globulin, and partly anti-androgenic effects (e.g. with the use of cyproterone acetate). Hirsutism is less likely to respond to COCPs and usually requires higher doses of an anti-androgen.[10]

The relationship between ovarian hormone production and premenstrual syndrome was suggested as early as 1931 and it has been common practice to treat premenstrual syndrome with COCPs to inhibit ovulation. However, no satisfactory controlled studies supporting the effectiveness of this treatment have been published.[11]

COCPs are not as effective in preventing transmission of sexually transmitted infections (STIs) as in preventing pregnancy. Although they reduce the risk of acute upper genital tract pelvic inflammatory disease,[12] they do not prevent cervical colonisation and those women at risk of encountering STIs are best advised to use condoms as well as COCPs.

Prevention of gynaecological and other disease

Possible small associations between COCPs and breast or cervical cancer have been given extensive publicity.[13] By contrast, the very high degree of protection offered to COCP users against endometrial and ovarian cancer, is much less well-known.

The long-term risk of ovarian cancer is reduced by 40% after 4 years of COCP use, 54% after 8 years, and 60% after 12 years.[14] Protection against ovarian and endometrial cancer continues for many years after discontinuation of COCP use[15] and appears to be related to the progestogenic component of the pill.[16] Case-control studies also show reasonably sound evidence that long-term use of COCPs provides some protection against the later development of uterine fibroids, endometriosis, recurrent ovarian cysts, acute pelvic inflammatory disease, infertility, iron-deficiency anaemia, benign breast lumps, toxic shock syndrome, acne and hirsutism.[17]

There is less substantial evidence for beneficial effects in reducing the later incidence of thyroid disease, rheumatoid arthritis, duodenal ulceration, *Trichomonas vaginalis* infection, and in assisting long-term maintenance of bone mineral density.

COCP use greatly reduces the risk of infertility[18] (presumably through protection against acute pelvic inflammatory disease, ectopic pregnancy and endometriosis). In many of these conditions, benefits become more marked with longer duration of COCP use.

Evidence of efficacy of COCP in preventing other conditions is summarised in Table II.

Conclusion

Modern, very low dose COPC pills, have maintained a high degree of contraceptive efficacy, but the margin for error in pill taking appears to be much smaller. These COCPs have a much lower incidence of side effects and serious complications than early high dose COCPs. Serious health risks from venous thrombo-embolism are rare, and not measurably higher for pills containing third-generation progestogens compared with earlier progestogens.

Most women feel confident taking modern COCPs but myths about these drugs still persist. Most non-contraceptive health benefits of COCPs are not widely appreciated, in spite of much evidence. Controversy still persists over the association between COCP use and breast cancer. Although slightly more breast cancers are detected in current COCP users (relative risk 1.24; 95%CI: 1.15-1.33), they are less advanced in stage and less aggressive in behaviour.

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Table II: Evidence for preventing gynaecological and other conditions with COCPs

Condition	Relative risk of developing condition after 5 years of COCP use	Evidence for greater degree of protection with longer COCP use*	NHMRC level of evidence[6]
Endometrial cancer	0.4	Strong	III-2
Ovarian cancer	0.6	Strong	III-2
Colon cancer	Evidence conflicting	Weak	IV
Acute pelvic inflammatory disease	0.5	None	II
Endometriosis	0.7	Weak	III-2
Uterine fibroids	0.8	Strong	III-2
Infertility	0.5	Weak	III-2
Recurrent ovarian cysts	0.5	Weak	III-2
Benign breast disease	0.5	Strong	III-2

COCP combined oestrogen-progestogen oral contraceptive pill
Changes in absolute risk cannot be reliably calculated
NHMRC National Health and Medical Research Council

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