



COMBINED ORAL CONTRACEPTIVES AND CARDIOVASCULAR DISEASE

Changes over the years in the composition of combined oral contraceptives (COCs), and improvements in the selection and monitoring of users, have helped ensure that very few women experience cardiovascular problems while using this popular method of contraception.

Arterial risks

Arterial disease is rare in pre-menopausal women, and most events occur in women not using COCs. At all ages, smoking poses a greater threat to the cardiovascular health of women than COC use.

Studies of myocardial infarction (MI) have found inconsistent results, perhaps because of varying levels of risk factors in the populations examined. Nearly all of any increased risk of MI in COC users occurs in women with other cardiovascular risk factors which include smoking, raised blood pressure (BP), diabetes mellitus or abnormal lipid levels. Users without these risk factors have little or no increased risk of MI, whatever their age. COC users have an increased risk of ischaemic stroke, again mostly in those with other risk factors (notably smoking, hypertension and history of migraine). COC use is also associated with a modestly elevated risk of haemorrhagic stroke, but mainly in women older than 35 years. A history of hypertension may exacerbate this effect.

All of the arterial risks occur while women use COCs. There is little if any relationship with duration of use, and the risks reduce once COCs are stopped. Progesterone only oral contraceptives are sometimes given to women with cardiovascular contraindications to COCs. Of the few studies that have examined the cardiovascular effects of progesterone only preparations, none have found an increased risk.

Data about the arterial risks of specific COC formulations are sparse. Given that most women stop COCs before they are likely to develop arterial disease, any differences between products are of marginal clinical importance.

Venous risks

Numerous studies have found an elevated risk of venous thromboembolism (VTE) among current users of low-oestrogen dose COCs. The effect appears to be stronger during the first year of use before falling to a smaller, but still elevated, risk that continues until COCs are stopped. The risk disappears rapidly after stopping. Women using COCs containing the progestogen, desogestrel or gestodene, probably have a higher risk of VTE than those using preparations containing other progestogens, particularly levonorgestrel. Although a number of explanations have been postulated for these differences, empirical evidence for these explanations is weak. In any event, the differences are small; perhaps 30 cases each year of venous thrombosis per 100,000 users of desogestrel or gestodene containing preparations compared with 15 per 100,000 users of other low-dose COCs.

Age, smoking and varicose veins are not important risk factors for VTE in COC users; obesity may elevate the risk although the evidence is contradictory. COC users with hereditary clotting factors, such as factor V Leiden mutation, have a substantially raised relative risk of VTE.

Blood pressure

Some women have a rise in BP while using a COC, including those using newer preparations. The effects tend to be modest, rarely leading to hypertension. Most changes reverse within a few months of stopping COC use.

Recommendations

- The arterial risks of COCs can be minimised, and possibly eliminated, by taking a careful personal and family history (with particular emphasis on cardiovascular and thromboembolic risk), and by checking the potential user's BP.
- Smokers wishing to use COCs should be encouraged to stop, although in young women the additional risk from smoking will be minimal.

- Recommendations about the frequency of monitoring BP are arbitrary. Before; 3, 6 and 12 months after starting; and annually thereafter seems reasonable. Hypertensive women should probably use another method of contraception.
- In the absence of smoking or hypertension, women with other cardiovascular risk factors might use COCs, but this advice is not based upon a substantial body of evidence. The presence of multiple risk factors should lead to greater caution and the consideration of alternative methods of contraception.
- The routine screening of all COC users for clotting abnormalities is not recommended, partly because current tests are poor discriminators between women who will, and who will not, develop a VTE.
- Ideally COCs should be stopped 4 weeks before major elective surgery and all surgery to the legs. Good alternative contraceptive arrangements should be made. COCs can be restarted at the first menses occurring at least 2 weeks after full mobilisation. If discontinuation of a COC is not possible or has not occurred, thromboprophylaxis is recommended. This advice does not apply to minor surgery of short duration or to women using progestogen only contraceptives.

Further reading

1. Hannaford PC, Webb AMC on behalf of an International Workshop. Evidence-guided prescribing of combined oral contraceptives. Consensus Statement. *Contraception* 1996; 54: 125-9.
2. WHO Scientific Group on Cardiovascular Disease and Steroid Hormone Contraception. Cardiovascular disease and steroid hormone contraception: report of a WHO scientific group. WHO technical report series: 877. Geneva WHO 1998.
3. Hannaford P. Cardiovascular events associated with different combined oral contraceptives. A review of current data. *Drug Safety* 2000; 22: 361-371.
4. Kemmeren JM, Algra A, Grobbee DE. Third generation oral contraceptives and risk of venous thrombosis: meta-analysis. *BMJ* 2001; 323: 1-9.
5. Factfile 2/2002 - Thrombophilia