The Effects of Combine Oral Contraceptive Pills on Cardiovascular Risk Factors: A Systematic Review on Clinical Trials

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Abstract

The combine contraceptive pills (COCPs), included a combination of esterogen and progesterone, are an accepted therapeutic for pregnancy prevention. Several studies indicated that COCP intake might have some side effects, such as cardiovascular diseases (CVD). Therefore this study aimed to investigate the effects of COCP on CVD risk factors.

Google Scholar, PubMed and Magiran Library databases were systematically searched to find relevant clinical trials investigating the effects of COCPs on CVD from inception up to June 2020.

Included articles (n = 10) assessed several risk factors such as blood pressure, serum levels of total cholesterol, triglyceride, low-density lipoprotein (LDL) and high-density lipoprotein (HDL). A total of the articles indicated the increament of blood pressure, serum levels of cholesterol, triglyceride, LDL and reduction in HDL following COCPs intake.

About 9% of women of reproductive age worldwide use oral contraceptives. This percentage rises to 18% of women in developed countries and 28% of women in the United Kingdom. Combined oral contraceptives form a substantial proportion of these, particularly in more developed nations. Although combined oral contraceptives are generally effective in preventing pregnancy, they have measurable side effects such as venous thromboembolism (VTE). VTE is important, not only because of the prolonged time over which women might be exposed to such contraceptives, but also because VTEs are potentially avoidable and can be fatal.

Previous studies have shown varying risks for different types of oral contraceptives (such as third generation pills compared with first or second generation pills), but such studies were done some years ago, and tended not to include new preparations containing drospirenone. Also, previous studies have generally had insufficient power to analyse the risks for more recent formulations such as norgestimate. Few studies—only four of those referenced here have included any detailed analyses of dosage and, of these, only Lidegaard and colleagues have covered a full range of prescribed drugs. Some studies did not control for all potential confounders (such as body mass index or smoking), while others analysed only healthy users. Different methodological approaches in studies have also made it difficult to compare and combine the results.15 Therefore, although the increased VTE risk associated with combined oral contraceptive drugs is established, the relative risks associated with different combinations remain inconclusive, especially for newer formulations.

The UK has some of the largest sources of routinely collected data in the world, with longitudinal primary care records spanning up to 25 years and linked to secondary care data and mortality records. These databases cover many millions of patients, include data both on exposure and outcomes, and therefore are representative of the setting in which drugs are used. This makes the databases ideally suited to large scale safety studies of commonly used drugs. In this study, we have used the two largest of these databases, QResearch (www.qresearch.org) and Clinical Practice Research Datalink (CPRD, www.cprd.com). Both have been used for earlier studies of associations between drug prescribing and VTE risks.

Our objective was to quantify the associations between use of combined oral contraceptives and risk of VTE, adjusting for comorbidities and other available confounding factors. In particular, we were interested to analyse risks associated with newer or less used preparations such as drospirenone or norgestimate, quantify risks associated with various types of progestogen, and analyse the effect of different doses of oestrogen on VTE risks. To make the study more comparable with previous studies, we also replicated analyses for different subgroups by age and health status and for VTE cases with anticoagulation prescriptions.

The results of studies showed that COCP intake for long time is related to the increase of the CVD risk factors and most probably they have an adverse effects on cardiovascular disease.

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