Steroidal contraceptives and bone fractures in women: evidence from observational studies

06 August 2013

An updated version of this systematic review has been published and can be found online at www.cochrane.org. We will soon update the below RHL summary to reflect the updated findings of the systematic review.

RHL Summary

Overall, observational studies show that oral contraceptives are not associated with increased risk of bone fractures. However, in certain subgroups of women, such as those have used the method longer than 10 years, there could be a greater fracture risk. Depot medroxyprogesterone acetate also increases the risk of fractures, while the hormonal intrauterine device appears to be protective.

Cochrane review


Abstract

Age-related decline in bone mass increases the risk of skeletal fractures, especially those of the hip, spine, and wrist. Steroidal contraceptives have been associated with changes in bone mineral density in women. Whether such changes affect the risk of fractures later in life is unclear. Hormonal contraceptives are among the most effective and most widely-used contraceptives. Concern about fractures may limit the use of these effective contraceptives. Observational studies can collect data on premenopausal contraceptive use as well as fracture incidence later in life.

We systematically reviewed the evidence from observational studies of hormonal contraceptive use for contraception and the risk of fracture in women.

In May 2012, we searched for observational studies. The databases included MEDLINE, POPLINE,
Cochrane Central Register of Controlled Trials (CENTRAL), LILACS, EMBASE, CINAHL, and Web of Science. We also searched for recent clinical trials through ClinicalTrials.gov and the ICTRP. For other studies, we examined reference lists of relevant articles and wrote to investigators for additional reports.

We included cohort and case-control studies of hormonal contraceptive use. Interventions included comparisons of a hormonal contraceptive with a nonhormonal contraceptive, no contraceptive, or another hormonal contraceptive. The primary outcome was the risk of fracture.

Two authors independently extracted the data. One author entered the data into RevMan, and a second author verified accuracy. We examined the quality of evidence using the Newcastle-Ottawa Quality Assessment Scale (NOS), developed for case-control and cohort studies. Sensitivity analysis included studies of moderate or high quality based on our assessment with the NOS.

Given the need to control for confounding factors in observational studies, we used adjusted estimates from the models as reported by the authors. Where we did not have adjusted analyses, we calculated the odds ratio (OR) with 95% confidence interval (CI). Due to varied study designs, we did not conduct meta-analysis.

We included 14 studies (7 case-control and 7 cohort studies). These examined oral contraceptives (OCs) (N=12), depot medroxyprogesterone acetate (DMPA) (N=4), and the hormonal intrauterine device (IUD) (N=1). This section focuses on evidence from the six studies with moderate or high quality evidence that we included in the sensitivity analysis.

All six studies examined oral contraceptive use. We noted few associations with fracture risk. One cohort study found OC ever-users had increased risk for all fractures (reported RR 1.20; 95% CI 1.08 to 1.34). However, a case-control study with later data from a subset reported no association except for those with 10 years or more since use (reported OR 1.55; 95% CI 1.03 to 2.33). Another case-control study reported increased risk only for those who had 10 or more prescriptions (reported OR 1.09; 95% CI 1.03 to 1.16). A cohort study of postmenopausal women found no increased fracture risk for OC use after excluding women with prior fracture. Two other studies found little evidence of association between OC use and fracture risk. A cohort study noted increased risk for subgroups, such as those with longer use or specific intervals since use. A case-control study reported increased risk for any fracture only among young women with less than average use.

Two case-control studies in the sensitivity analysis also examined progestin-only contraceptives. One reported increased fracture risk for DMPA ever-use (reported OR 1.44 (95% CI 1.01 to 2.06), more than four years of use (reported OR 2.16; 95% CI 1.32 to 3.53), and women over 50 years old. The other noted increased risk for any past use, including one or two prescriptions (reported OR 1.17; 95% CI 1.07 to 1.29), and for current use of 3 to 9 or 10 or more prescriptions. In addition, one study reported reduced fracture risk for ever-use of the hormonal IUD (reported OR 0.75; 95% CI 0.64 to 0.87) and longer use of that IUD.

Observational studies do not indicate an overall association between OC use and fracture risk. Some reported increased risk for specific user subgroups. DMPA users may have an increased fracture risk. One study indicated hormonal IUD use may be associated with decreased risk. Observational studies need adjusted analysis because the comparison groups usually differ. Researchers should be clear about the variables examined in multivariate analysis.

Source URL: https://extranet.who.int/rhl/topics/fertility-regulation/contraception/steroidal-contraceptives-and-bone-fractures-women-evidence-observational-studies
Published on RHL (https://extranet.who.int/rhl)

Home > Steroidal contraceptives and bone fractures in women: evidence from observational studies