JOURNAL CLUB

Hormonal contraception and bone mineral density

A prospective, controlled study of the effects of hormonal contraception on bone mineral density. Berenson AB, Radecki RM, Grady JJ, Rickert VI, Thomas A. *Am J Obstet Gynecol* 2001; **98**: 576–582.

This prospective controlled study compared the effects of depot medroxyprogesterone acetate (DMPA) and two types of combined oral contraception (COC) on bone mineral density (BMD). Over 12 months, users of DMPA experienced a mean loss of 2.74% in BMD at the lumbar spine. This compared with a 0.33% loss for women not using hormonal contraception and small increases (0.33–2.33%) for users of the two pills studied.

The cases were women who were eligible for US military training, and were similar to volunteer controls in age, ethnicity, body mass index (BMI), intake of dietary calcium, and whether or not they regularly undertook weight-bearing exercise. The authors themselves point out that as the all the women had a high school degree, were within 36% of their ideal body weight, and most were white, the results may not be generalisable to the US population.

All participants were recruited from a larger contraceptive study and their baseline bone density measurements were done as part of that study. The women themselves self-selected the type of contraception they would use for the duration of the study. Those who chose DMPA were about twice as likely to be smokers as those who chose the COC. Those women who chose COC were randomised to either 'red' or 'green' formulations. The purpose of this is not clear, but may have been part of the larger study design. The women who chose non-hormonal contraception were recruited as controls. BMD was measured within 2 months of choosing a contraceptive method and 10–14 months later.

Discontinuation rates were high for hormonal contraception, leading to fewer than 50% of users of hormonal contraception having follow-up data for analysis (compared with 83% of controls). Intention-to-treat analysis was not used. Power calculations were performed post hoc. Statistical analysis was carried out after correcting for confounding variables that may themselves have an effect on BMD.

The main finding, that DMPA is associated with a reduction in BMD over 12 months, confirms most previous work in the area. Why cigarette smokers are more likely to choose injectable contraception remains unclear. The differences between different oral preparations warrant further investigation. The other interesting finding was that, despite this being a relatively healthy group of subjects, only 7–12% of women reported adequate calcium intake. This is a public health point that may well be generalisable to our own practice.

Reviewed by **Dr Pauline McGough**, MBBS, DFFP
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Non-contraceptive use for Depo-Provera

Depot medroxy progesterone acetate: a poor preparatory agent for endometrial resection. Kriplani A, Manchanda R, Monga D, Takkar D. *Gynecol Obstet Invest* 2001; **52**: 180–183.

This small randomised study looked at the use of Depo-Provera as a preparatory agent prior to endometrial resection. This may be clinically useful if operation time and postoperative bleeding patterns were improved. The study was small with only 25 women in each of two groups. Computer randomisation was carried out in women attending with subjective heavy menstrual blood losses; who had completed their family; whose uterus was less than 12 weeks' size; and in whom a bleeding disorder was excluded. The outcomes of the study were subjective. Clinicians described the visual appearance of the endometrium and measured thickness with the end of the hysteroscope. All procedures were carried out successfully but it is unclear if this was by one or more surgeons. Endometrial thickness was known prior to surgery. Clinicians were not blinded to the randomisation. Patients were followed up for 4 years after their surgery and outcomes measured were a subjective improvement in menstrual symptoms and satisfaction. However, it is not clear if the control group received intramuscular placebo or if they too were not blinded. Mean operative time was longer at 37.1 min in those pretreated compared to 33.6 min in the control group. Amenorrhoea was achieved in only 28% (7) of the pretreated group compared to 40% (10) of the untreated group. Hypomenorrhoea/spotting occurred in 60% (15) of the pretreated group and in 56% (14) of the untreated group. This study concluded that Depo-Provera was a poor endometrial preparatory agent but larger studies should be carried out to confirm this.

Reviewed by **Dr Susan Brechin**, MRCOG, DFFP
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Venous thromboembolism and cyproterone acetate

Risk of venous thromboembolism with cyproterone or levonorgestrel contraceptives. Vasilakis-Scaramozza C, Jick H. *Lancet* 2001; **358**: 1427–1429.

This important study addressed the reasonable suspicion that combined oral contraceptive pills (COCs) containing cyproterone might be more thrombogenic than those containing progestogens. Cyproterone COCs combine an oestrogen and an anti-androgen, making them more oestrogenic than other COCs and therefore perhaps more thrombogenic.

The researchers used an established design to construct a case-control study extracting data from the General Practice Research Database. Total study population was 99 401 women aged 16–39 years who had received a prescription for cyproterone- or levonorgestrel-containing COCs. In this group, 26 women had a probable diagnosis of idiopathic venous thrombo-embolism (VTE) and a current or very recent prescription for those COCs. The researchers identified 144 controls, matched for age (and GP practice, where possible).

This study could be affected by confounding factors if women using cyproterone COCs are different from those using levonorgestrel (LNG) COCs. The analysis therefore controlled for smoking, body mass index (BMI), acne, hirsutism, polycystic ovarian syndrome (PCOS) and asthma.

The relative risk of VTE on cyproterone pills was estimated at 3.9 times the risk on a LNG pill. The 95% confidence intervals were wide at 1.1–13.4. Duration of pill use did not seem to affect risk of VTE.

This study draws on a large pool of data about women using the pill in real life and is therefore widely generalisable. The results support a biologically plausible effect that has also been supported by other studies. Larger studies on this effect are unlikely to be practical so we need to advise women on the basis of these figures. Women using cyproterone COCs are looking for therapeutic effects as well as reliable contraception. Higher levels of risk are acceptable in this situation. The increased risk of VTE must be discussed with women using these pills, just as with women who opt to use third-generation pills. The data sheet for cyproterone pills suggests women should use them until symptoms resolve, then try changing to other COCs. These results support this practice.

Reviewed by **Dr Kate Weaver,** DFFP
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Risk factors for breast cancer

Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58 209 women with breast cancer and 101 986 women without disease. The Collaborative Group on Hormonal Factors in Breast Cancer. *Lancet* 2001**; 358:** 1389–1399.

This is an important meta-analysis from the Collaborative Group on Hormonal Factors in Breast Cancer. Previous data from this analysis has been published on the risk of hormonal contraception and hormonal replacement therapy on the risk of breast cancer. This study included 58 209 women with invasive carcinoma of the breast and 101 986 women without disease. Fifty-two studies (including two unpublished studies) were included with at least 100 women in each study. Results would be generalisable. Although retrospective, recall of carcinoma in mother, sister(s) or daughter(s) is likely to be good by the very nature of the diagnosis. For women in more developed countries the estimated cumulative incidence of breast cancer up to the age of 50 years is 1.7% with no affected first-degree relative, 3.7% with one and 8% with two. The estimated incidence of breast cancer up to the age of 80 years was 7.8% with no affected first-degree relatives, 13.3% with one and 21.1% with two. The estimates for deaths from breast cancer up to the age of 80 years are 2.3% with no affected relatives, 4.2% with one and 7.6% with two. Clinically this is relevant to our clients since 8/9 women developing breast cancer will not have an affected first-degree relative. Although those women with a first-degree relative are at increased risk the majority will never develop the disease. In countries where breast cancer is common, the lifetime excess risk with one first-degree relative affected is 5.5% and for two is 13.3%.

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Genetic risk counselling by GPs

Evaluation of the impact of two educational interventions on the GP management of familial breast/ovarian cancer cases: a cluster

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randomised controlled trial. Watson E, Clements A, Yudkin P, et al. *Br J Gen Pract* 2001; **51:**817–821.

Should basic risk assessment and genetic counselling become part of primary care to ensure appropriate referral of only medium- to high-risk patients, and to provide the necessary reassurance to low-risk patients?

In an attempt to answer this question, this article refers to a study performed in 1999 in which the impact of both an information pack on general practitioner (GP) management of familial breast/ovarian cancer, and also an in-practice educational session was assessed.

A 62% response rate was achieved from the 688 GPs in all practices in Oxfordshire and Northamptonshire. The pack was found to lead to improved referral decisions in the short term. Whilst the in-house education session increased reported confidence, it lead to no additional improvement in referral decisions.

Even in the group of GPs receiving both pack and education sessions, less than one-third felt confident in counselling and management.

The authors suggest that genetic risk counselling is a new role for the GP, and that practical risk counselling sessions might be required before GPs are expected to provide such a service.

Reviewed by **Penny Watson**, MFFP, MPH
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Relationship counselling role for health visitors

A randomised controlled trial of training health visitors to identify and help couples with relationship problems following a birth. Simons J, Reynolds J, Morison L. *Br J Gen Pract* 2001; **51:** 793–798.

The early postnatal phase is recognised to be a potentially difficult time of adjustment for parents. This study in 1997 in a London borough followed health visitors trained in a 4-day 'Brief Encounters' course, who then administered an eight-item Relationship Dynamic Scale questionnaire at 6–8 weeks postpartum to women thought to have a partner. Such women were twice as likely than the control group to have revealed a relationship problem, and 75% more likely to have received help. (All health visitors in the study and the control group, incidentally, continued to administer the Edinburgh Postnatal depression survey, and 50% of mothers were found to be depressed.)

The authors suggest that this intervention may be a useful way for primary care teams to respond to such problems that often have serious consequences for family well-being. Time restrictions are recognised to be the main barrier for its use however. Health visitors trained in relationship counselling may be more able to treat postnatal depression. (Interestingly, no measure of the parity of the women was made in this study, nor mention made of use of contraception!)

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