The pill, parity and cervical cancer risk

Two papers carried out by the International Agency for Research on Cancer (IARC) were published recently in The Lancet (2002). They aimed to investigate evidence of a link between long-term oral contraception (OC), increasing parity, human papilloma virus (HPV) and cervical cancer. These important papers address the growing suspicion that reproductive factors such as parity and contraception may affect the risk of cervical cancer. Certainly this is biologically plausible, since both pregnancy and combined oral contraception maintain the transformation zone on the ectocervix where it is exposed to co-factors such as HPV. Previous publications suggesting a link have been unable to exclude confounding factors such as sexual behaviour.

IARC pooled analysis of 10 case-control studies. These studies were performed in underdeveloped countries with high-risk populations for cervical cancer such as Morocco, Brazil, Peru, Paraguay and Colombia; with intermediate-risk populations such as Thailand and the Philippines; and low-risk populations such as Spain. These case-control studies compared histologically verified cases of invasive cervical cancer and carcinoma in situ, with age-matched control women drawn largely from hospital populations. HPV was found in 1465 (95.6%) of women with invasive squamous cell cancer, 211/292 women (72%) with in situ cancer, 124/135 women (92%) with adenocarcinoma or adenosquamous carcinoma and 225/1939 (12%) control women. The study was performed using unconditional logistic regression models and associations of exposures were assessed with likelihood ratios. Variables such as sociodemographic factors, sexual history, contraceptive use, smoking, lifetime history of cervical screening, history of sexually transmitted infection, and effects of obstetric history were ascertained by trained interviewers using a standardised questionnaire.


This first paper aimed to investigate evidence of a link between cervical cancer, human papilloma virus (HPV) and long-term oral contraception (OC). Women were tested for presence of HPV DNA in cervical smears. HPV infection is now accepted as an important factor in the aetiology of cervical cancer. These papers therefore restrict their analyses to women who tested positive for HPV. A total of 1676 cases were included. Including HPV-negative women, who are essentially not at risk of cervical cancer, would have reduced the chance of detecting any genuine link between cervical cancer and OC use. There were only 255 controls, leaving the study vulnerable to selection bias. Around 40% of the HPV-positive women had high-risk HPV types. Restricting analysis to these women did not significantly alter the findings. Both squamous and adenocarcinoma in situ were considered. Researchers analysed data using complex statistical models aimed at taking account into possible confounding factors such as age at first intercourse and age at first pregnancy. An association between increasing duration of OC use and risk of cervical cancer and carcinoma in situ was identified. No association was found with age at first OC use. Use of OC for less than 5 years was not associated with increased risk of cervical neoplasia. Women with a total of 5 to 9 years of OC use had almost three times the risk of cervical neoplasia (odds ratio 2.82, 95% CI 1.46–5.42). Those women with more than 10 years of OC use had four times the risk of cervical neoplasia (odds ratio 4.03, 95% CI 2.10–7.92). The increased risk of cervical neoplasia appeared to persist for as long as 15 years after discontinuing OC. Use of OC itself did not appear to increase the chance of infection with HPV.

This study would appear to confirm a plausible association between OC and cervical cancer. Researchers focused on women deemed at high risk of developing cervical cancer because they were HPV-positive. These findings cannot therefore be explained away by higher risk sexual activity as has been done previously. It must be acknowledged, however, that there are a number of areas where bias may have been introduced. Recall bias is acknowledged in that women may have been more likely to recall previous use of hormonal contraceptive methods and some may have used progesterone-only methods. Only one HPV test was carried out, but persistence of HPV is thought to be an important factor in carcinogenesis. The authors did not distinguish those women who had only transient infection from those with persistent HPV. Although the findings are relevant for women in the developed world, most of the women in the study (apart from those from Spain) lived in countries in which there are no national cervical screening programmes. This study serves to underline the importance of attending for regular cervical screening smears. In this context, these findings need not affect women’s contraceptive or reproductive choices. In discussion with women in the UK, it is important to stress the much lower rates of cervical cancer here, in addition to the many benefits of OC use and attending for routine cervical screening.

Reviewed by Dr Kate Weaver, MB CB, DFFP


This second paper looked at parity acting as a co-factor, with oncogenic strains of human papilloma virus (HPV), to cause neoplasia of the cervix. This study was carried out in 83 institutions in 21 countries with similar methodology as the previous study. Women aged between 18 and 40 years. The study was open and non-randomised because women had very strong preferences for postnatal contraception and were allowed to choose their preferred method. The study was described as group-comparative: women were included into two groups, either using 75 µg desogestrel-only progestogen pill or a copper intrauterine contraceptive device (IUD). The researchers aimed to look at the quantity and quality of breast milk in these two groups of women. In a small subset of women they also looked at the levels of etonogestrel (the active metabolite of desogestrel) in breast milk and maternal serum. In addition researchers assessed infant growth and wellbeing until the age of 30 months.

This was a small study was carried out in 83 women aged between 18 and 40 years. The study was open and non-randomised because women had very strong preferences for postnatal contraception and were allowed to choose their preferred method. The study was described as group-comparative: women were included into two groups, either using 75 µg desogestrel-only progestogen pill or a copper intrauterine contraceptive device (IUD). The researchers aimed to look at the quantity and quality of breast milk in these two groups of women. In a small subset of women they also looked at the levels of etonogestrel (the active metabolite of desogestrel) in breast milk and maternal serum. In addition researchers assessed infant growth and wellbeing until the age of 30 months.

Desogestrel-only pill and breastfeeding

Desogestrel-only pill and breastfeeding


This was a small study was carried out in 83 women aged between 18 and 40 years. The study was open and non-randomised because women had very strong preferences for postnatal contraception and were allowed to choose their preferred method. The study was described as group-comparative: women were included into two groups, either using 75 µg desogestrel-only progestogen pill or a copper intrauterine contraceptive device (IUD). The researchers aimed to look at the quantity and quality of breast milk in these two groups of women. In a small subset of women they also looked at the levels of etonogestrel (the active metabolite of desogestrel) in breast milk and maternal serum. In addition researchers assessed infant growth and wellbeing until the age of 30 months.
Kate Weaver

J Fam Plann Reprod Health Care 2002 28: 164
doi: 10.1783/147118902101196405

Updated information and services can be found at:
http://jfprhc.bmj.com/content/28/3/164.1.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/