

Preconceptional factors in the prediction of fertility and the reproductive lifespan

July 1 2014

A project in Denmark whose aim is to assess the reliability of preconceptional lifestyle and biological factors as predictors of fertility has found a pronounced effect of the contraceptive pill on markers used to assess "ovarian reserve", a predictor of future reproductive lifespan. Available evidence of whether the Pill has an effect on fertility has so far been reassuring - and usual advice to those stopping the Pill is that cycles will soon revert to normal, with pregnancy likely within six months or so.(1)

However, one continuing concern for those taking the Pill long-term is its effect on reproductive status and whether this is masked by the Pill. Now, a new study reported today at the ESHRE Annual Meeting in Munich by Dr Kathrine Birch Petersen from the Copenhagen University Hospital in Denmark indicates that the Pill has a marked suppressive effect on two well established markers of ovarian reserve, which are each considered reliable predictors of ovarian ageing and onset of menopause.

In recent years the term "ovarian reserve" has been used to describe the ability of the ovary to produce follicles and mature oocytes capable of fertilisation. And ovarian reserve is today most accurately assessed by two simple measurements: levels of anti-Mullerian hormone, or AMH, in the blood; and the number of early (antral) follicles in the ovary. AMH is measured in a blood test, and antral follicles counted when visualised by a vaginal ultrasound (AFC). A combination of AMH and AFC is today considered the best test of ovarian reserve and future reproductive

lifespan - and thus an indicator of the biological clock's current status. As both parameters have been shown to change with age, AMH and AFC have been recognised as markers of ovarian ageing.

Now, the Danish study has found that measurements of AMH and AFC were 19% and 16% respectively lower in Pill users than in those not taking the Pill. In addition, ovarian volume was also significantly smaller - by between 29 and 52%, with the greatest reductions seen in the group aged 19-29.9 years.

The study, which included 833 women (aged 19-46 years) attending the Fertility Assessment and Counselling Clinic at Copenhagen University Hospital from August 2011 to April 2014, compared measures of AMH, AFC and ovarian volume in users and non-users of the Pill. Almost 30% of them were former Pill users. The study was part of a wider project to test whether preconceptional assessment of biological, medical and lifestyle factors is able to predict future fertility and duration of reproductive lifespan, to decrease the need for fertility treatments and to provide information to women on their likelihood of natural conception.

"We expected to find an effect of the Pill," said Dr Birch Petersen. "But during the project we were surprised at the quantified effect on ovarian reserve parameters as defined by anti-Müllerian hormone, antral follicle count and ovarian volume." Even after statistical adjustment for age, BMI, smoking, maternal age at menopause, maternal smoking during pregnancy and prematurity, AMH was still up to 30% lower and AFC up to 20% lower in Pill users than in non-Pill users.

The results, said Dr Birch Petersen, suggest that measurements of AMH and AFC in the assessment of reproductive status must be modified in those taking the Pill. "However," she added, "we do not believe that the Pill changes the ovaries in any permanent way. But we still need to know more about the recovery phase after women stop the Pill. The Pill is

unlikely to change the basal ovarian biology of egg depletion – but it certainly changes the appearance of the ovaries and the secretion of AMH."

As a result, said Dr Birch Petersen, women in the preconceptional care programme in Copenhagen who have been on the Pill "are now advised that their ovaries may look old, with small volume, a few small antral follicles and low levels of AMH". But this she added, may not necessarily reflect her future fertility status.

Consequently, in order have a more precise measurement of the biological clock's status and to reassure the Pill user about her fertility potential, ovarian reserve assessment might be repeated three months after stopping the [pill](#). The Pill may mask a severely diminished [ovarian reserve](#), she said, and this is important to recognise.

More information: Abstract O-203: Ovarian reserve assessment in users of oral contraception seeking fertility advice on their reproductive time span

Notes

1. For example, a study of almost 60,000 Pill users in 2009 found that of those stopping the Pill for a planned pregnancy 21.1% were pregnant after one cycle and 79.4% at one year (13 cycles). Hormone type and dose, duration of use, and parity had no major influence on the rate of pregnancy, and age, up 35 years, had only a minor influence (Cronin M, Schellschmidt I, Dinger J. Rate of pregnancy after using drospirenone and other progestin-containing oral contraceptives. *Obstet Gynecol* 2009; 114: 616-22).

Provided by European Society of Human Reproduction and Embryology

Citation: Preconceptional factors in the prediction of fertility and the reproductive lifespan (2014, July 1) retrieved 19 April 2024 from

<https://medicalxpress.com/news/2014-07-preconceptional-factors-fertility-reproductive-lifespan.html>

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