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EDITORIAL

Oral contraceptives: 40 years after release

ØJVIND LIDEGAARD

About 40 years ago, oral contraceptives (OCs) were released in Scandinavia. Few medicinal products can exhibit similar impressive key figures as OCs. Less than 4 years after their release, more than one-third of all women of reproductive age were on the pill. The sale of OCs has fluctuated through the years, but has steadily increased through the last decade, and today more than half of all young women are taking the pill. Globally, more than 80 million women are on the pill (1). These figures express one vital circumstance-the majority of women on the pill experience more good than harm with its use.

As the majority of women on the pill are healthy, the requirements for an essentially safe product are higher than for medicines administered for more or less serious diseases. For the same reason, few medicinal products have been investigated so intensively and continuously as OCs. Therefore, we have gathered precise risk and benefit estimates for a long list of clinical outcomes in relation to OCs.

The results of all these scientific contributions is that the most significant short-term risk is a 3–4 times increased risk of venous thromboembolism (VTE). In young, except pregnant, women this disease is rare, therefore even a few times increased risk is still a low absolute and acceptable risk. The majority of young women suffering a VTE (with or without OCs) survive with no or few long-lasting symptoms.

While the risk of VTE has not changed much through the development of new low-dose and less androgenic OCs, the previously several fold increased risk of arterial thrombotic complications has been reduced, but not eliminated.

Despite overwhelmingly reassuring epidemiological evidence through many years, it has been difficult to eliminate the fear of an increased risk of cancer with long-term use of OCs. The well documented increased risk of breast cancer in women on hormone therapy after the menopause has contributed to this concern. The situation for postmenopausal women is, however, quite different from the situation in women of reproductive age. In the former case, we add hormones to women producing only small amounts of sex steroids themselves. In the latter case, we replace endogenous hormones with external synthetic hormones. Therefore, an increased risk of breast cancer with hormone therapy in older women does not imply an increased risk of cancer in young women with OC use.

Recently, Hannaford et al. published a long-term follow-up on women on OCs in the late 1960s and early 1970s, confirming that there is no overall long-term cancer risk with even prolonged use of OCs (2). On the contrary, the overall cancer risk in ever-users of OCs was significantly reduced by 12%. These results are in line with previous publications. Nevertheless, such long-term follow-ups are important in order to eliminate the final concerns that may have survived more than 100 reassuring scientific publications on the issue.

Focusing on sub-types of cancer according to the new study, women on OCs have a decreased risk of endometrial and ovarian cancer by approximately 40–50%, have an unchanged risk of breast cancer, a 28% reduced risk of colorectal cancer, and a 33% increased risk of cervical cancer. In addition, with the new vaccine against HPV, there is a good possibility of reducing this risk in the future. Until it is proven that vaccination provides complete and long-term protection against cervical cancer, women on OCs should undergo regular cervical cancer screening.

What about a possible increased risk of breast cancer in women starting OC use at an early age, as recently suggested in a Swedish study (3)?

First, these results were restricted to women with a genetic predisposition (BRCA 1/2), and to those who developed breast cancer before the age of 36 years. Secondly, these women are often also at an increased risk of developing ovarian and colon

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cancer, risks which are effectively reduced by OCs. The same study confirmed that OC use after 20 years did not confer any increased risk of breast cancer in women. Therefore, this report does not justify any specific caution with OCs.

Finally, millions of young women use a safe contraception, avoid unwanted pregnancies, are spared induced abortions, and experience less menstrual pain, bleeding and discomfort. In addition, OCs are effective in the treatment of women with PCOS and endometriosis. Soon we will be even more familiar with menstruation-free regimens of hormonal contraception. If we could develop hormone types or add substances that decreased the reduced sensitivity to activated protein C (APC-resistance), we would be approaching a near ideal hormonal contraceptive product.

Do gynecologists still have an input with regard to OCs? Yes, our job, in close collaboration with the work of GPs, is to ensure that the few women with absolute contraindications against OCs are advised against its use, and to choose and counsel women individually on the most appropriate contraceptive for her, considering her specific biological and social life circumstances. Furthermore, it is necessary for gynecologists to increase attention towards early signs of VTE, ensuring timely diagnosis and treatment for the few women who suffer from this complication.

For nearly 40 years, OCs in Scandinavia have had a profound influence on our contraceptive habits, reproduction and societies. It is difficult to imagine a future new product that during the next 40 years could bring a similar or bigger impact to the world.

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