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Editorial

Hormonal contraception and venous thromboembolic risk in midlife women

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Several new observational studies have assessed the risk of venous and arterial thrombosis in users of different types of hormonal contraception [1–5]. The new studies have confirmed that combined hormonal products have much more influence on venous thrombosis than they have on the arterial end points, thrombotic stroke and myocardial infarction. Thus, among users of combined oral contraceptives (COC) the risk of venous thrombosis is increased 3–6 times compared to non-users [1–3], while the risk of arterial thrombosis is increased 1.5–2 times [5].

With the withdrawal of 50 µg oestrogen COC from the market, the difference in thrombotic risk between middle and low-oestrogen COC is of less importance than the influence from different progestogen types. The 2nd generation COC with the progestogens levonorgestrel and norgestimate confer a three times increased risk of venous thrombosis, while COC with 3rd (desogestrel and gestodene) and 4th (drospirenone) generation progestogens increase the risk at least six times [1–3].

While the risk of venous thrombosis is highest during the first year of use, no trend according to length of use has been found for arterial thrombosis. After the first year of use, the risk of venous thrombosis is almost constant.

It is now confirmed in several independent studies that the transdermal contraceptive patch (EVRA) confers more than the double risk of venous thrombosis as compared to the corresponding 2nd generation combined pill with norgestimate [4], and at the same time also increases the risk of arterial thrombosis about three times [5]. The contraceptive vaginal ring (NuvaRing) increases the risk of venous thrombosis as much as 3rd and 4th generation COC, and the risk of arterial thrombosis about 2½ times. At the time in reproductive age where the incidence rates of venous and arterial thrombosis are highest, these two non-oral combined products should therefore generally be avoided.

On the other hand, progestogen only contraception including progestogen only pills with norethisterone or levonorgestrel, levonorgestrel releasing intrauterine system (LNG-IUS), subcutaneous implant (Implanon) or the oestrogen free pill with desogestrel, all these oral and non-oral products do not increase the risk of venous or arterial thrombosis. At the same time, some of these products have non-contraceptive benefits, which are more needed at this

time in women's reproductive live than earlier, e.g. the reduction in menstrual bleeding with use of LNG-IUS.

Many women get relative contraindications against combined hormonal contraception as they get older. At the same time as recognising these contraindications, it is also important to realise, that these contraindications do not apply to progestogen-only contraception. The newest and largest study on LNG-IUS has actually demonstrated a significant 43% decrease in risk of confirmed venous thrombosis as compared to non-users [4], in agreement with a 19% reduction in the sex hormone-binding globulin (SHBG) with this treatment; SHBG is considered as a surrogate marker for the risk of venous thrombosis in users of hormonal contraception.

It has been normal practice for years to consider contraindications against combined hormonal contraception as contraindications against all hormonal contraception. This era should with the new studies be definitively over. Thus women who are smokers, or with hypertension, hyperlipidaemia, migraine, adiposity, diabetes, family disposition for thrombotic diseases, or with hypercoagulation disorders, could all safely take progestogen only contraception.

Some clinicians would go a step further. Why not recommend all women on combined oral contraceptives a LNG-IUS when they pass 35 years? A woman on a 3rd or 4th generation pill will thereby reduce her risk of venous thrombosis with 90% and of arterial thrombosis with 65%, and women on a 2nd generation product the risk of venous thrombosis with 83% and the same 65% reduction of arterial thrombosis. Not a bad option at a time where the incidence rate of especially the arterial complications increases exponentially and rapidly with further increase in age. At the same time such a shift would imply other non-contraceptive benefits, including the prevention of many bleeding complications during the following decade in such a woman's life.

Although few per cent of women on LNG-IUS experience a pressure mood with LNG-IUS, this risk is probably much lower in women who have had good compliance with the progestogen dominated combined oral contraceptives.

Instead of trying to refute new scientific insights from large-scale epidemiological studies, the clinicians should implement the new knowledge into their practice, and let our patients benefit from our new more nuanced picture of hormonal contraception and thrombotic risk.

Contributors

Øjvind Lidegaard is the contributor to this article.

Competing interests

The author has within the last three years received honoraria for speeches in pharmacoepidemiological issues, including fees from Bayer Pharma Denmark, and MSD Denmark, and has been expert witness for plaintiff in a legal US case in 2011–2012.

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