OCs and VTE: a practical answer to an old question

In a recent commentary in this journal, Jürgen Dinger1 argued that “the risk of VTE [venous thromboembolism] attributable to COCs [combined oral contraceptives] is a class effect, primarily dependent on the dose of estrogen” and that the type of progestogen used in the COC probably does not influence this risk. In an editorial in the British Medical Journal that accompanied the publication of the two largest studies to date on this topic, Nick Dunn2 concluded: “All of the more recent progestogens, possibly except nogestomet, might seem to be at a disadvantage with regard to VTE”.

As VTE is a very rare event, it is unreasonable to expect the answer to the progestogens and VTE question from a randomised controlled trial. We may thus never be able to exclude residual confounding as a possible explanation for the higher VTE rates found with newer progestogens. Luckily in clinical practice this does not matter much. For OCs, as for any treatment, health professionals should first recommend the safest and most effective treatment, and in the absence of known differences between treatments we should then consider costs.

Most patients requesting a COC request it solely for contraception. Most of these patients will be correctly initiated on a COC containing a second-generation progestogen, usually levonorgestrel (LNG). Dr Dinger does not question that COCs containing LNG are at least as safe and effective as those containing one of the newer progestogens.

The basket of care offered by sexual health services is constantly changing. More than was the case in the past, we promote subdermal and intrauterine methods and offer sexually transmitted infection (STI) and HIV screening and manage genital tract infection. To afford to do this we have to keep costs as low as possible. Where budgets are finite and probably shrinking, the cost of prescribing COCs containing a newer progestogen instead of LNG can be measured in fewer implants or intrauterine methods inserted and fewer chlamydia or HIV tests undertaken.

This is as good a reason as any to adhere to Faculty Guidance on First Prescription of Combined Oral Contraception, which states: “A monophasic COC containing 30 µg ethinyl estradiol with norethisterone or levonorgestrel is a suitable first pill (Grade C)”1.

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References

Reply
To respond to the letter from Dr Pittrof and Sauer,1,2 the two articles published in the British Medical Journal3,4 assessed the risk of venous thromboembolism (VTE) associated with the use of oral contraceptives (OCs), and in particular the role of the type of progestogen. My commentary5 addressed the methodological strengths and weaknesses of these two studies. It did not seek to preferential prescribing of certain progestogens or groups thereof. This would also not be possible on the basis of VTE risk, because it is quite conceivable that progestogens do not differ at all or do differ only slightly in terms of their VTE risk, but could well differ with respect to other risks – for example, of arterial thromboembolic events such as acute myocardial infarction and stroke.

In addition, the situation may be different with regard to a number of pharmacological characteristics, such as anti-androgenic and anti-mineralocorticoid properties. While manufacturers’ sales organisations and regulatory agencies may emphasise or even overemphasise differences in the pharmacological profiles of progestogens, that does not mean that these differences are negligible in clinical practice.

At a time when it is becoming increasingly difficult to finance health care, cost-conscious use of pharmaceutical products should not be a taboo topic – especially if these products are not paid for by the patients or users themselves. This applies, for example, to OCs in the UK – in contrast to the vast majority of other countries. Here I would agree with Drs Pittrof and Sauer. However, I am also explicitly in favour of discussing and critically examining safety concerns that are published about certain groups of OCs yet that are of debatable scientific merit – independently of the price on these products. Any other position on this matter would be scientifically questionable as well as irresponsible. The debate surrounding second- and third-generation OCs has made us all aware of how easily questions about safety can be fuelled with all too fabled ‘pill scare’ that does not remain focused on a certain group of products but instead leads to an overall drop in OC use. That can, in turn, lead to increased abortion rates, and does a disservice to women who do not wish to become pregnant.

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References

Drosopirenone and VTE

Following publication in the October 2009 issue of the commentary article regarding the risk of venous thromboembolism (VTE) with combined oral contraceptives (COCs) and subsequent criticisms,1 we would like to share some information regarding prescribing in Zagreb, Croatia of a recently introduced COC, containing 3 mg drosopirenone and 30 µg ethinyl estradiol (DROSPEE) (Yasmin®). We collected data in the city of Zagreb during the period 2004–2008, employing various data sources as follows: data on inpatients from Zagreb; data on the causes of hospitalisation; data on side effects from the Agency for Drugs and Medicinal Products; and data on drug use from Zagreb pharmacies. The total female population under surveillance was 37 841 in 2004 and 40 577 in 2008, yielding a 3.2-fold increase. Other annual trends in the overall utilisation of COCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase. Other annual trends in the overall utilisation of COCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase. Other annual trends in the overall utilisation of COCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase. Other annual trends in the overall utilisation of COCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase. Other annual trends in the overall utilisation of COCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase.

In Zagreb, use of COCs in general increased from 28.9% in 1999 to 57.7% in 2008. The rate of hospitalisation for VTE, which continued to decrease, suggest that there is no correlation between these two parameters.

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Filshie clip migration and retention

We wish to advise journal readers about an unusual case of Filshie clip migration and retention inside the uterine cavity that to our knowledge has never been reported before.

A 68-year-old woman, with three previous vaginal births, presented with postmenopausal bleeding for 2 weeks. She underwent a laparoscopic Filshie clip sterilisation 25 years ago and had been menopausal for 16 years. An ultrasound scan suggested an endometrial polyp that was confirmed on hysteroscopy. A closed Filshie clip was seen within the uterine cavity and attached to the polyp by fibrous adhesions. The clip was removed along its longitudinal axis with forceps after dilating the cervical os. The right os was not evident except for a small dimple at its expected site. Histology confirmed a benign endometrial polyp.

The clip was lying relatively freely inside the uterine cavity without being expelled. The likely sequence of events could have been a low-grade foreign body inflammatory reaction that resulted in incorporation and subsequent burrowing of the clip through the uterine wall into its cavity. Burrowing and migration through the Fallopian tube is also a possibility and could explain the closure of the right os by post-inflammatory adhesions.

Laparoscopic sterilisation with Filshie clip remains a popular method of permanent contraception since its introduction by Marcus Filshie in 1981. It is a safe procedure, with a failure rate of 1 in 200.1 The 12.7 mm long and 4 mm wide titanium clip is lined with silicone rubber and is closed round the Fallopian tube by means of an applicator leading to avascular tubal necrosis. The tube eventually divides and the stumps heal leaving two occluded ends.2 The clip usually remains attached to the site of tubal separation and becomes detached when a delay is in peritonealisation, the clip may become detached and migrate through tissue planes. This is estimated to occur in 0.6 per 1000 cases.3 Directly attached clips are most commonly found within the peritoneal cavity, typically in the Pouch of Douglas or the paracolic gutters. Migration to the urinary bladder, vagina, rectum and into the perineum leading to an ischiorectal abscess has

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