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 norgestimate, now 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 COCs, as for any treatment, health professionals should first recommend the safest and most effective treatment, and in the absence of knowledge about differences between treatments we should then consider costs.

Most patients requesting a COC request it solely for contraception. Most of these patients will be perfectly satisfied with 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 as 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 genitral 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)”3.

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References

Drospirenone and VTE

Following publication in the October 2009 issue of the commentary article regarding the risk of venous thromboembolism (VTE) with combined oral contraceptives (OCs) and subsequent criticisms,1,2 we would like to share some information regarding prescribing in Zagreb, Croatia of a recently introduced OC, containing 3 mg drospirenone and 30 μg ethinylestradiol (DRSP/EE) (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 hospitalization; data on the 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 approximately 250,000.

In Zagreb, use of OCs in general increased by 31% between 2004 and 2008. This rising tendency was especially pronounced after 2005, when the combination DRSP/EE was introduced. In 2005, DRSP/EE accounted for 15.4% of the overall utilisation of OCs, which increased to 57.7% in 2008, yielding a 4.4-fold increase. Other OCs classified as fixed combinations of progestogens and estrogens showed a decrease in

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 by a very minor degree in 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, we would point out that the type of progestogen used in OCs is a class effect, being different with regard to a number of pharmacological characteristics, such as anti-androgenic and anti-mineralocorticoid properties. While manufacturers’ sales organisations will undoubtedly emphasise the 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 pharmacological 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. I would like to draw attention to the possible consequences of this and the possible risk of regulatory agencies overemphasising differences in the pharmacological profiles of progestogens, that does not mean that these differences are negligible in clinical practice.

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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 flimsy adhesions. The clip was removed along its longitudinal axis with forceps after dilating the ostium. The ostium 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 possible and could explain the closure of the right ostium by post-inflammatory adhesions.

Laparoscopic sterilisation with Filshie clip remains a popular method of permanent contraception since its introduction by Marcus Filshie in 1981.1 It is a simple 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 invisible. If 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 Direct contact with the clip is 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 peritoneum leading to an ischiorectal abscess has