LETTERS TO THE EDITOR

OCSs 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, may 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 consider 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 happy 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 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 genit al 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.

Rudiger Pittrof, MSc, MRCOG
Consultant, Enfield Community Services, Reproductive and Sexual Health (RASH), London, UK
E-mail: rudiger.pittrof@enfield.nhs.uk

Ulrike Sauer, MD
Specialist Registrar, Enfield Community Services, Reproductive and Sexual Health (RASH), London, UK

References

Reply

To respond to the letter from Dr Pittrof and Sauer,1,2 the two articles published in the British Medical Journal,3,4 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 in a minor way in their effect on VTE 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 progestogen effect may be different with regard to a number of pharmacological characteristics, such as anti-androgenic and anti-mineralocorticoid properties. While manufacturers’ sales organisations increasingly stress the need to 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 pharmacutical 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 Dr 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 and may only differentially price these products. Any other position on this matter would be scientifically questionable as well as irresponsible. The debate surrounding second- and third-generation OCSs has made us all aware of how easily questions about safety can become a full-fledged ‘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, does a disservice to consumers and professionals, as it is also self-defeating for the safety of women who do not wish to become pregnant.

Jürgen Dinger, MD, FRCOG
Director, Berlin Centre for Epidemiology and Health Research, Berlin, Germany.
E-mail: dinger@cgz-berlin.de

References

Drosopirenone and VTE

Following the 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 drospirenone and 30 µg ethinyl estradiol (DROS/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 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 approximately 250,000.

In Zagreb, use of COCs in general increased in 2005, DRSP/EE accounted for 15.4% of the contraceptive market (1,457 of 9,526 registered). In 2008, DRSP/EE made up 16.6% of the contraceptive market (2,038 of 12,263 registered). This increase was particularly pronounced after 2005, with a tendency to further increase (see Table 1).

Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>DRSP/EE %</th>
<th>COCs %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>15.4</td>
<td>91.3</td>
</tr>
<tr>
<td>2005</td>
<td>16.6</td>
<td>86.4</td>
</tr>
<tr>
<td>2006</td>
<td>17.9</td>
<td>84.8</td>
</tr>
<tr>
<td>2007</td>
<td>19.3</td>
<td>82.6</td>
</tr>
<tr>
<td>2008</td>
<td>21.3</td>
<td>79.6</td>
</tr>
</tbody>
</table>

In Zagreb, use of DRSP/EE is issued on private prescription by pharmacies. COCs are usually prescribed by gynaecologists, but may also be prescribed by other specialists.

The number of reported side effects of all drugs of any kind increased by 69.2% (i.e. from 993 in 2005 to 1680 in 2008). Annual trends in the rate of hospitalisation for VTE, which continues to remain at very low levels, suggest that there is no correlation between these two parameters.

Marcel Leppär, MD, PhD
Specialist in Public Health, Department of Pharmacoepidemiology, Andrija Stampar Institute of Public Health, Zagreb, Croatia.
E-mail: marcel.leppar@stampar.hr

Mirela Eric, MD, MSc
Plastic Surgeon, Department of Anatomy, School of Medicine, University of Novi Sad, Novi Sad, Serbia

Josip Culig, MD, PhD
Professor, Department of Pharmacoepidemiology, Andrija Stampar Institute of Public Health, Zagreb, Croatia

Reference

Filshie clip migration and retention

We wish to advise journal readers about an unusual case of Filshie clip migration and retention inside the ureteric 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 ureteric cavity and attached to the polyp by filmy adhesions. The clip was removed along its longitudinal axis with forceps after gentle traction. The double J stent with a Hirst ring in the right ostium was not evident except for a small dimplke at its expected site. Histology confirmed a benign endometrial polyp.

The clip was lying relatively freely inside the ureteric 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 ureteric wall into its cavity. Burrowing and migration through the Fallopian tube is also a possibility 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. It is a safe and effective method, 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 once in a delay in peritonealisation, the clip may become detached and migrate through tissue planes. This is estimated to occur in 0.6 per 1000 cases.3 Dislodged clips are most commonly found within the peritoneal cavity, typically in the Pouch of Douglas or the paraotic glands. Migration to the urinary bladder, vagina, rectum and into the perineum leading to an ischiorectal abscess has