UPDATE ON COMBINED ORAL CONTRACEPTIVES: RISK OF VENOUS THROMBOEMBOLISM. DROSPIRENONE *VERSUS* OTHER PROGESTINS

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Background

The risk of venous thromboembolism (VTE) associated with combined oral contraceptives (COCs) is well known, but the relation with progestin-type is controversial.

Purpose

✓ To describe a suspected deep vein thrombosis (DVT) associated with drospirenone (DRSP)-containing COCs.
✓ Literature review about VTE risk of DRSP versus other progestins.

Methods

- Medical record review.
- Literature search of Medline

MeSH terms used:
Oral contraceptives hormonal, combined oral contraceptives, drospirenone, drospirenone and ethinyl-estradiol combination, progestins, thromboembolism, venous thromboembolism, drug toxicity.

Results

1) Case report

- 36-year-old woman
- Obstretics history: G_4 A_2 V_2, dysmenorrhea, ovarian cysts and fibroadenoma.
- Non-smoker
- No known drug allergies
- User of NSAIDs and COCs

COCs used:

Edelsin®: 2007-March 2010: 35 mcg EE/250 mcg norgestimate

↓

Gestinyl®: March-November 2010: 20 mcg EE/75 mcg gestodene

↓ Stopped due to methorragia

Yaz®: Novembre 2010-August 2011: 20 mcg EE/3 mg DRSP

EE: ethinyl-estradiol

On August 2011, she was attended in an Internal Medicine Outpatient Consultation after a previous admission in which radiological test ruled out DVT, although D-dimer (DD)=1220 ng/mL.

The physician decided her readmission to hospital due to persistent induration and pain in right calf (DD= 571 ng/mL).

DVT was suspected again and a **confirmatory doppler ultrasound** was performed. Low molecular weight heparin was initiated, followed by acenocoumarol.

She was discharged [medium compression stockings, acenocoumarol and analgesics]. COC was stopped and derived to Gynecology Outpatient Consultation.

Suspected adverse drug reaction (ADR) was reported to the regional center of Pharmacovigilance.

2) Literature review

Thrombotic risk in users of a DRPS-conteining COCs relative to users of preparations conteinind levonorgestrel (or other progestins).

Autor, year	Study design	Adjusted rate ratio (95% CI) DRSP *vs* levonorgestrel	Adjusted *odds* ratio (95% CI) DRSP *vs* levonorgestrel
Seeger, 2007[1]	Cohort	0,9 (0,5-1,6)	X
Dinger, 2007[2]	Cohort	1 (0,6-1,8)*	X
Lidegaard, 2009[3]	Cohort	1,64 (1,27-2,10)	X
van Hylckama,2009[4]	Case-control	X	1,7 (0,7- 3,9)
Jick, 2011[5]	Nested case-control	2,8 (2,1-3,8)	2,4 (1,7-3,4)
Parkin, 2011[6]	Nested case-control	2,7 (1,5-4,7)	3,3 (1,4-7,6)

* Other progestins

In 2011, Food and Drug Administration and European Medicines Agency warned that DRSP-conteining COCs may be associated with an incresead risk of VTE.

Conclusions

The result of spontaneous reporting of ADR can improve the safety profile of drugs. Our case adds further information to the recently published epidemiological studies that suggest an increased risk of VTE associated with DRSP.

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