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MeReC Publications

Observational studies find increased VTE risk with Yasmin

Two observational studies (UK study[1] and US study[2]) found a two to three-fold increased relative risk of venous thromboembolism (VTE) associated with the use of combined oral contraceptives (COCs) containing drospirenone (e.g. Yasmin), compared with COCs containing levonorgestrel. This translated to about 20 to 30 cases of VTE per 100,000 women-years of use with COCs containing drospirenone and about 10 cases per 100,000 women-years of use with COCs containing levonorgestrel. However, this risk of VTE with COCs is less than that associated with pregnancy (about 60 cases per 100,000 pregnancies).

Action

Health professionals should review their prescribing of oral contraceptives to ensure it reflects updated MHRA advice. The VTE risk with COCs containing drospirenone (e.g. Yasmin) is higher than with COCs containing levonorgestrel, and may be similar to that of COCs containing desogestrel or gestodene. Although patient choice is an important factor in selecting a suitable contraceptive, a COC containing levonorgestrel is a sensible choice for a woman who decides to start or switch contraception, because of levonorgestrel's well known safety profile.

So what?

The MHRA has advised that COCs containing levonorgestrel have the lowest thrombotic risk and are the safest COC for a woman who wants to start or switch contraception. However, all COCs increase the risk of VTE and there is no reason for women to stop taking COCs containing drospirenone, or any other COC, on the basis of these findings.

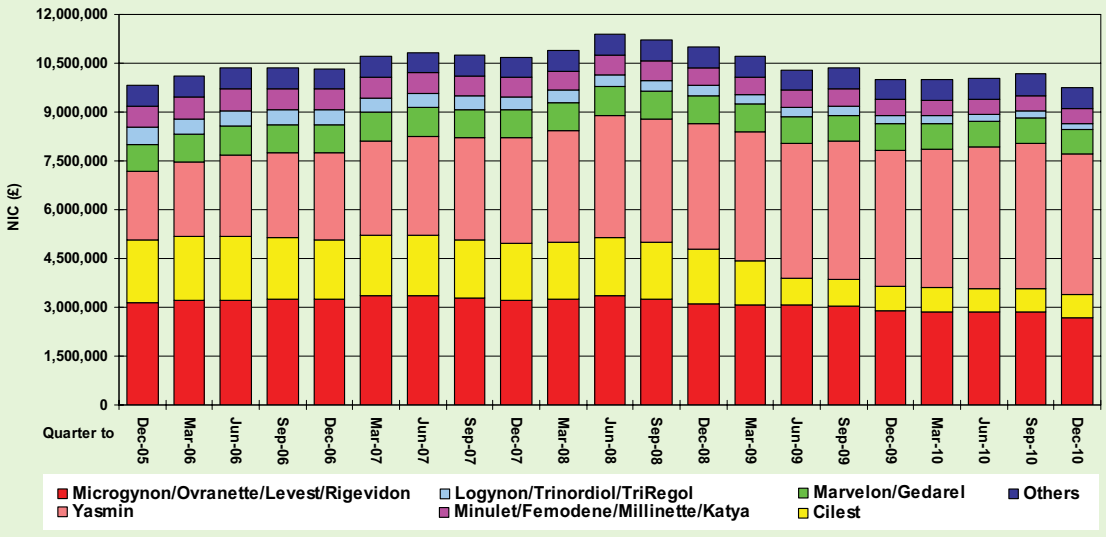
Yasmin is expensive compared with other COCs (excluding Qlaira▼), and in the quarter to December 2010 accounted for about £18 million of the £40 million annual spend in general practice in England (see **Figure 1**). As there is no conclusive evidence that Yasmin is clinically superior to other COCs with regard to non-contraceptive effects (e.g. fluid retention, premenstrual symptoms), this amount of prescribing could be viewed as excessive.

See MeReC Rapid Review No. 3549 for further study details. More information can be found in the NPC e-learning materials on contraception.

References

1. Parkin L, et al. BMJ 2011;340:d2139
2. Jick SS, Hernandez RK. BMJ 2011;340:d2151

Figure 1. Trends in spending on standard strength COCs in general practice in England



All information was correct at the time of publication (August 2011)

New study doesn't change role of leukotriene receptor antagonists in asthma

A pragmatic randomised study[1] found that a leukotriene receptor antagonist (LTRA) was equivalent to an inhaled corticosteroid (ICS) as first-line preventer therapy, and to a long-acting beta$_2$ agonist (LABA) as add-on therapy to ICS, in adults with asthma. However, this study has important limitations and does not change current recommended practice.

Action

Health professionals should continue to follow the recently revised SIGN/BTS asthma guideline. For patients not adequately controlled on a short-acting beta$_2$ agonist (SABA) when required (step 1), ICS remain the first choice regular preventer therapy (step 2). An LTRA may be considered in children under five years if an ICS cannot be used.

A proportion of patients with asthma may not be adequately controlled on an ICS alone at step 2. For adults, adolescents and children aged 5 to 12 years, evidence supports that the addition of a LABA to an ICS should be considered next (step 3). For children under five years, the first choice add-on therapy to an ICS is an LTRA. However, before adding or changing treatment, practitioners should check concordance with existing therapy, check the patient's inhaler technique and eliminate trigger factors where possible.

What does this study claim?

This study claimed that an LTRA was equivalent to ICS as first-line preventer therapy (n=306) and also to LABA as add-on therapy (n=352) in primary care patients. The pre-defined equivalence criteria were met at two months (based on Mini Asthma QoL Questionnaire [miniAQLQ] scores), but not at two years. There were no significant differences in asthma exacerbation rates and Asthma Control Questionnaire (ACQ) scores.

So what?

The body of evidence supports SIGN/BTS recommendations that ICS are the first-choice preventer therapy for people with asthma, and LABAs are the first-choice add-on therapy to ICS for people with asthma aged five years and over. Pragmatic studies have strengths and weaknesses, and the interpretation of the results of this study may be problematic, particularly due to the lack of a placebo group and crossover between treatment groups – for example, patients in the LTRA groups received more treatment changes than the other group. For more details of the study, including further discussion of its limitations see MeReC Rapid Review No. 3847. For more information see the NPC e-learning materials on asthma.

Reference

1. Price D, et al. N Engl J Med 2011;364:1695–707

Cardiovascular risks with calcium and vitamin D: re-analysis of data

Re-analysis of data[1] from a large RCT found a modest increase in the risk of some cardiovascular events in postmenopausal women using calcium and vitamin D supplements to prevent osteoporotic fractures. This is in contrast to the authors' conclusions from the initial analysis of the original study, who found no increased risk. The finding appears to be supported by inclusion of previously unpublished data from other studies in a meta-analysis. However, there are limitations to the data which make its implications unclear.

Action

Regulatory agencies including the MHRA have considered the relevant data, and **no change to prescribing practice is currently recommended**. Unless and until the MHRA publish advice on this matter, prescribers should consider these data in discussions with patients and weigh the potential benefits and risks of using calcium and vitamin D on an individual basis. They should do so in line with NICE guidance on primary and secondary prevention of osteoporotic fracture, which recommends prescribers should consider offering these supplements to postmenopausal women who receive treatment (e.g. with bisphosphonates) unless they are confident that the patient has an adequate calcium intake and is vitamin D replete. Prescribers may also consider offering calcium (at least 1g/day depending on nutritional calcium intake) plus vitamin D (700–800 units/day) to people not receiving pharmaceutical treatment or prophylaxis, but who are at high risk of falls or fractures such as frail elderly people living in care homes.

For more details on this study and its limitations see MeReC Rapid Review No. 3859.

Reference

1. Bolland M, et al. BMJ 2011;342:d2040

Risk of atypical fractures with bisphosphonates

Two observational studies (one in Canada[1] and another in Sweden[2]) have reported an increased risk of atypical femoral fractures in older women taking bisphosphonates, which increases with duration of use. However, in absolute terms, this risk may be considered quite low, and far lower than the number of osteoporotic fractures prevented. Following a Europe-wide review, the MHRA has advised that atypical femoral fractures is considered a class effect of bisphosphonates, and the overall balance of risks and benefits remains favourable.

Action

Health professionals, and patients taking bisphosphonates, should follow recent MHRA advice taking note that:

- atypical fractures may occur rarely in the femur, especially after long-term use
- the need for continued treatment with bisphosphonates should be re-evaluated periodically (especially after five or more years of use), although the optimum duration of treatment has not been established
- patients taking bisphosphonates should be advised to report any thigh, hip, or groin pain, and any patients reporting these symptoms should be evaluated for an incomplete femur fracture
- if an atypical fracture is suspected in one leg then the other leg should also be examined
- discontinuation of the bisphosphonate should be considered while patients suspected to have an atypical femur fracture are evaluated.

In addition, health professionals should continue to follow NICE guidance on primary and secondary prevention of osteoporotic fracture and the detailed MHRA guidance on all other safety considerations with bisphosphonates.

See the June 2011 edition of Drug Safety Update for more information and MeReC Rapid Review No. 3896 for details of the two studies. Further information can also be found in the NPC e-learning materials on osteoporosis and in MeReC Bulletin 2010;20(1).

References

1. Park-Wyllie LY, et al. JAMA 2011;305:783–9
2. Schilcher J, et al. N Engl J Med 2011;364:1728–37

The National Prescribing Centre (NPC) is responsible for helping the NHS to optimise its use of medicines. NPC is part of the National Institute for Health and Clinical Excellence (NICE), an independent organisation providing national guidance on promoting good health and preventing and treating ill health.

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