How does VTE risk for the patch and vaginal ring compare with oral contraceptives?

Evidence-based answer
Evidence is conflicting with regard to the comparative frequency of venous thrombotic events (VTE) among women using the transdermal patch when compared to an oral contraceptive (OC), even though the patch produces a relatively high serum ethinyl estradiol (EE) level (strength of recommendation [SOR]: C, conflicting cohort case-control studies). The vaginal ring has a risk of VTE comparable to that of an OC (SOR: B, 1 comparative study).

Clinical commentary
For now, base decisions on patient preference This review points out that we don’t have enough evidence to make a strong recommendation about oral or nonoral estrogen-containing contraceptives based on the risk of thromboembolic disease. All estrogen-containing contraceptives have similar side-effect profiles, regardless of the route of administration.

In my experience, the patch or ring appeals to women who have had difficulty with OCs and need a simpler dosing regimen to improve compliance. The choice between an oral estrogen-containing contraceptive and the patch or ring should be based on the patient’s preference, not the risk of thromboembolic disease, until we have evidence to suggest otherwise.

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Evidence summary
Two nonoral estrogen-progestin contraceptives have been approved by the US Food and Drug Administration (FDA). OrthoEvra is a transdermal patch applied weekly for 3 consecutive weeks, followed by 1 patch-free week per cycle. The NuvaRing is a vaginal ring worn for 3 consecutive weeks in a 4-week cycle.

The patch causes greater estrogen exposure than OCs or the ring
In November 2005, the FDA issued an update to the labeling of the OrthoEvra contraceptive patch, reporting increased systemic estrogen exposure, which may increase the risk of blood clots. The FDA warned that the transdermal patch exposes the user to 60% more estrogen than the typical birth control pill containing 35 μg EE. In January 2008, the FDA approved an additional update to include the results of a new study that found users of the patch to be at higher risk of developing VTE than OC users.
VTE risk

One pharmacokinetic study found that exposure to EE differed among delivery groups. At least 7 days should be allowed after stopping EE before starting an MAO inhibitor. CYP2D6 and CYP2C19. For patients with severe or life-threatening allergic reactions to ergot alkaloids, other ergot derivatives, or any component of this product, discontinue immediately.

Treatment and consider tapering EREX XR in the first trimester. Laser, Delivery, Nursing: The effect on labor and delivery outcomes is unknown. Voriconazole and IDR have been reported to be tetrahydrobiopterin in humans. Because of the increased risk of QT-interval prolongation, EREX XR is not recommended for use during the first trimester of pregnancy. In animal studies, EREX XR caused fetal deformities and was embryotoxic at doses higher than those achieved in humans by clinical use. There is no established risk from maternal clonidine use during pregnancy. The overall health of neonates born to mothers who used clonidine during pregnancy is unknown. Clonidine use during pregnancy should be considered where the benefits outweigh the risks. In U.S. clinical trials, there were no reports of withdrawal symptoms in infants whose mothers had used clonidine in pregnancy. Reconsider the use of EREX XR during pregnancy in view of the potential for serious adverse effects on the fetus. It is not known whether EREX XR is distributed in human milk. EREX XR should not be used during breastfeeding. EREX XR has not been shown to be effective in the treatment of premature labor�

GROUP INSURANCE RECOMMENDATIONS

Group insurance should be a part of any medical plan. It is important to consider the following factors when evaluating a group insurance plan:

- Coverage for inpatient and outpatient services
- Coverage for prescription drugs
- Coverage for mental health services
- Coverage for dental services
- Coverage for vision care
- Coverage for alternative medicine services

The following questions should be considered when reviewing a group insurance plan:

1. What is the premium cost for the group insurance plan?
2. What is the network of providers available under the group insurance plan?
3. What is the deductible and copay amount for inpatient and outpatient services?
4. What is the annual limit on prescription drug coverage?
5. What is the out-of-pocket maximum for mental health services?
6. What is the out-of-pocket maximum for dental services?
7. What is the out-of-pocket maximum for vision care?
8. What is the out-of-pocket maximum for alternative medicine services?

One situation in which a group insurance plan may be particularly useful is when an individual has a chronic illness or a condition that requires ongoing medical care. In such cases, a group insurance plan may provide more comprehensive coverage than an individual insurance plan. Group insurance plans are available from employers, unions, and other organizations. It is important to shop around and compare different group insurance plans to find the one that best meets the needs of the individual.
ing factors. The incidence of VTE in this study was 40.8 per 100,000 women-years among patch users and 18.3 per 100,000 women-years among users of the norgestimate-35 μg EE OC. The study reported a more than 2-fold increased risk of VTE in patch users compared to OC users (OR=2.4; 95% CI, 1.1–5.5; IRR=2.2; 95% CI, 1.3–3.8).5,7

**Do the differences between studies make a difference?**

The 2 studies appear similar in design but have 2 major identifiable differences:

- The first study verified VTE diagnoses by claims for systemic anticoagulants, whereas the second study expanded its analysis by performing confirmatory chart reviews for VTE diagnoses.
- The first study included only new OC and patch users as of April 1, 2002, whereas the second study included new and experienced users of the OC as of April 1, 2002.

The significance of the differences in these studies is debatable; the results have yielded controversial, conflicting evidence.

**Safety and tolerability are similar for the vaginal ring and OCs**

A 1-year, open-label, randomized Phase III study of 1030 women compared the NuvaRing with a combination OC containing levonorgestrel and 30 μg EE. One case of deep venous thrombosis occurred in the NuvaRing group.

In reviewing the data, the authors concluded that the NuvaRing demonstrated comparable safety and tolerability to the OC.5 NuvaRing users experienced similar side effects compared with OC users.9

**Recommendations**

The World Health Organization Medical Eligibility Criteria for Contraceptive Use (WHOMEC) reports that long-term safety data for the estrogen-progestin contraceptive patch are not available.10 However, the limited studies that are available suggest a safety profile similar to that of combination OCs with comparable hormone formulations.

WHOMEC suggests that the guidelines for combination OCs also should apply to the patch and the ring. Women shouldn’t use these contraceptive methods if they have a history of VTE or current VTE or if they are undergoing major surgery that may include prolonged immobilization.10

**References**