Causes of intermenstrual bleeding in a woman on oral contraceptives not related to pill type

<table>
<thead>
<tr>
<th>Missed pill</th>
<th>Tobacco use</th>
<th>Pregnancy-related issues, including ectopic pregnancy</th>
<th>Infection – cervicitis, endometritis, and specifically chlamydia, gonorrhea, trichomonas</th>
<th>Cervical abnormalities – polyp, dysplasia, carcinoma</th>
<th>Endometrial abnormalities – polyp, hyperplasia, carcinoma; leiomyomas</th>
<th>Metabolic abnormalities – thyroid, prolactin, liver or renal failure, coagulation defects</th>
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Intermenstrual bleeding is defined as bleeding between periods and is common in the first 3 to 4 cycles of COC use. A narrative review recommends that other causes of bleeding should be considered before changing the COC (TABLE 1). A 2011 Cochrane review analyzed 21 RCTs (with about 10,000 women) comparing COCs containing ≤20 mcg ethinyl estradiol (EE) with those with >20 mcg EE. COCs containing ≤20 mcg EE had higher rates of irregular bleeding (one trial; N=778; OR 1.6; 95% CI, 1.4–4.4). Women who chose UAE had shorter procedures than either hysterectomy (one trial; N=156; mean difference [MD] −16 minutes; 95% CI, −26 to −6.8) or myomectomy (one trial; N=121; MD −50 minutes; 95% CI, −59 to −41), and resumed normal activities earlier (one trial; N=96; MD −26 days; 95% CI, −32 to −20). UAE was associated with shorter hospitalizations when compared with hysterectomy by 2.2 days (one trial; N=57; 95% CI, 1.6–2.8) to 4.1 days (one trial; N=57; 95% CI, 2.9–5.4). There was no statistical difference between surgery and UAE as far as ovarian failure (2 trials; N=297; OR 1.0; 95% CI, 0.53–1.9) or recurrence of fibroids (one trial; N=120; OR 1.3; 95% CI, 0.38–4.6). 1

What is the approach to intermenstrual bleeding in a woman taking a combined oral contraceptive?

Evidence-Based Answer

Causes of bleeding not related to combined oral contraceptive (COC) pill use should be considered first (SOR: C, expert opinion). If the bleeding is directly related to the COC, changing to a COC that contains >20 mcg ethinyl estradiol (EE) or a newer generation progestin may cause less intermenstrual bleeding. Altering the phasic formulation of progestin or changing between continuous and cyclic COC does not improve intermenstrual bleeding (SOR: B, systematic review with heterogeneous RCTs). 2

A 2011 Cochrane review evaluated 30 RCTs including nearly 14,000 women using a COC with 30 mcg EE to compare different generations of progestin (TABLE 2) and intermenstrual bleeding. 3 Women using a second-generation monophasic progestin were less likely to stop their COC due to cycle disturbances compared with a monophasic first-generation progestin (one trial; N=875; RR 0.69; 95% CI, 0.52–0.91) or a triphasic first-generation preparation (3 trials; N=581; RR 0.61; 95% CI, 0.43–0.85). Based on one double-blind RCT with unclear randomization of 456 women receiving a monophasic preparation over 6 cycles, women using gestodene (third generation) reported less bleeding than those using levonorgestrel (second generation) (RR 0.71; 95% CI, 0.55–0.91; NNT=8).

A 2006 Cochrane review evaluated the effect of phasic formulation of progestin on intermenstrual bleeding. 4 Only one trial of limited quality compared

a biphasic and monophasic progestin preparation. The study examined 533 user cycles of a biphasic pill (500 mcg norethindrone plus 35 mcg EE for 10 days, followed by 1,000 mcg norethindrone plus 35 mcg EE for 11 days) and 481 user cycles of a monophasic contraceptive pill (1,500 mcg norethindrone acetate plus 30 mcg EE daily). The study found no significant differences in intermenstrual bleeding between the monophasic and biphasic progestin formulations.

A 2011 Cochrane review compared continuous (>28-day use) with cyclic formulations of a COC, including 5 RCTs with a total of 765 women on continuous COCs and 416 on cyclic COCs. COCs given continuously had equivalent bleeding patterns compared with traditional cyclic dosing, although there was a slight improvement (not statistically significant) with continuous administration.

Evidence-Based Answer

Hypoglycemia is defined as a plasma glucose level (PGL) less than the fifth percentile. Fifth percentile values in normal term newborns are 28, 40, and 48 mg/dL at 1 to 2, 3 to 47, and 48 to 72 hours of life, respectively (SOR: B, meta-analysis of observational studies). However, blood glucose screening is not required in healthy term newborns, and blood glucose concentrations should be measured only in term infants who have clinical signs of hypoglycemia or who are considered “at risk.”

Neonates at risk for hypoglycemia and requiring screening and management include (i) small-for-gestational-age infants; (ii) large-for-gestational-age infants; (iii) infants of mothers with diabetes mellitus; and (iv) preterm infants (34–36 weeks’ gestation). The guidelines emphasize that the signs of neonatal hypoglycemia are nonspecific and include a wide range of signs and symptoms common in sick newborns, including jitteriness, cyanosis, seizures, apneic episodes, tachypnea, weak or high-pitched cry, floppiness or lethargy, poor feeding, and eye-rolling.

What is the best approach to screening for hypoglycemia in normal newborn infants?

Evidence-Based Practice learning objectives

1. To become knowledgeable about evidence-based solutions to commonly encountered clinical problems.
2. To understand how ground-breaking research is changing the practice of family medicine.
3. To become conversant with balanced appraisals of drugs that are marketed to physicians and consumers.