Cochrane for Clinicians

Putting Evidence into Practice

Heavy Menstrual Bleeding in Premenopausal Patients and the Role of NSAIDs

Anne Mounsey, MD, and Rita M. Lahlou, MD, MPH, University of North Carolina Department of Family Medicine, Chapel Hill, North Carolina

Author disclosure: No relevant financial affiliations.

Clinical Question

Do nonsteroidal anti-inflammatory drugs (NSAIDs) effectively reduce heavy menstrual bleeding in premenopausal patients?

Evidence-Based Answer

NSAIDs are effective for reducing heavy menstrual bleeding in premenopausal patients with menorrhagia when compared with placebo. However, NSAIDs are less effective than tranexamic acid (Cyklokapron) and the levonorgestrel-releasing intrauterine system (Mirena) for reducing heavy menstrual bleeding. Adverse effects of NSAIDs, particularly gastrointestinal effects, are variable in frequency, although typically not severe.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Menorrhagia, or heavy menstrual bleeding, is defined as 80 mL or more of menstrual blood loss per period, although in practice the diagnosis is based on patient report of an amount or frequency of blood loss that interferes with physical or psychosocial well-being. This common gynecologic problem affects 30% of patients of reproductive age. It is an important cause of health care resource utilization and a common condition seen in the primary care setting.[2,3] The authors of this Cochrane review sought to determine the safety and effectiveness of NSAID therapy for heavy menstrual bleeding in comparison with placebo and other common treatments.

This Cochrane review included 19 randomized controlled trials involving 759 premenopausal patients with heavy menstrual bleeding without a pathologic or iatrogenic cause.[1] One trial took place in Canada, 13 in Europe, two in Australia, and three in Asia, and they involved patients 12 to 55 years of age. The primary outcomes included subjective and objective menstrual blood loss. Because of differing study designs, the meta-analysis included nine trials with 419 patients; the other 10 trials were described individually.

Compared with placebo, mefenamic acid (Ponstel; 500 mg three times daily) taken from start to finish of menses resulted in fewer reports of heavy menstrual bleeding (absolute risk reduction = 56%; 95% CI, 38% to 69%; number needed to treat = 2; 95% CI, 1 to 3; n = 80). In another trial, mefenamic acid (500 mg three times daily) taken from five days before menses to cessation of bleeding reduced measured menstrual blood loss when compared with placebo (mean difference = –124 mL per cycle; 95% CI, –186 to –62; n = 11).

The remaining six of eight trials comparing NSAIDs with placebo were crossover trials; although data could not be pooled, five of six trials showed results favoring NSAIDs. Compared with placebo, mefenamic acid (500 mg three times daily) taken at onset of menses decreased blood loss by 16 to 23 mL in two studies (n = 38) but showed no difference in another (n = 15). Naproxen (250 mg two times daily and 500 mg two times daily) taken at the onset of menses reduced menstrual blood loss by 37 to 54 mL when compared with placebo (two studies; n = 18). Ibuprofen (400 mg three times daily) taken throughout the menstrual cycle decreased menstrual blood loss by 36 mL compared with placebo. Ibuprofen (600 mg daily) taken throughout the cycle did not decrease menstrual blood loss vs. placebo (one study; n = 13). The dosages of mefenamic acid in these studies were higher than the typical recommended dosing in the United States, which is a single dose of 500 mg, followed by 250 mg four times daily for up to three days. NSAIDs are contraindicated in patients with both heavy menstrual bleeding and bleeding disorders caused by platelet aggregation inhibition, and they carry an

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increased risk of serious cardiovascular thrombotic events and adverse gastrointestinal events, including bleeding.[4]

Tranexamic acid (1 g four times daily) taken for five days decreased menstrual blood loss compared with mefenamic acid (500 mg three times daily; mean difference = 73 mL per cycle) without a significant difference in subjective report of menstrual blood loss. The levonorgestrel-releasing intrauterine system significantly reduced median menstrual blood loss compared with NSAIDs (82 mL per cycle at three months; one study; n = 51). There was no significant difference in menstrual blood loss between NSAIDs (mefenamic acid, 500 mg three times daily) and ethamsylate (not available in the United States; 500 mg four times daily; two studies; n = 82), oral progesterone (norethindrone, 5 mg two times daily for eight to 10 days of the menstrual cycle; two studies; n = 48), and an oral contraceptive (ethinyl estradiol/levonorgestrel, 30 mcg/150 mcg daily for 21 of 28 days; one study; n = 26). These studies were mostly underpowered. The addition of NSAIDs to other medical treatments has not been well studied. Treatment with danazol is no longer recommended because of the risk of hepatotoxicity, thromboembolism, and intracranial hypertension.

The results of this review, although based on small and mostly underpowered studies without data amenable to pooling, are consistent with the recommendations from the National Institute for Health and Care Excellence, suggesting that the levonorgestrel-releasing intrauterine system be the initial treatment for heavy menstrual bleeding. Nonhormonal medications (tranexamic acid or NSAIDs) and other hormonal therapies (luteal phase progestins or combined oral contraceptives) are considered secondary options with similar effectiveness.[3] Desire for contraception, presence of dysmenorrhea, and comorbidities should be considered when discussing treatment options with individual patients.

The practice recommendations in this activity are available at http://www.cochrane.org/CD000400.

References

1. Bofill Rodriguez M, Lethaby A, Farquhar C. Non-steroidal anti-inflammatory drugs for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2019;(9):CD000400.
2. Fraser IS, Mansour D, Breymann C, et al. Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. *Int J Gynaecol Obstet*. 2015;128(3):196-200.
3. National Institute for Health and Care Excellence. Heavy menstrual bleeding: assessment and management. NICE guideline [NG88]. Last updated March 31, 2020. Accessed June 30, 2020. https://www.nice.org.uk/guidance/ng88
4. Kadir RA, Lukes AS, Kouides PA, et al. Management of excessive menstrual bleeding in women with hemostatic disorders. *Fertil Steril*. 2005;84(5):1352-1359.

Smoking Cessation with Text Messaging and App-Based Interventions

Elizabeth Salisbury-Afshar, MD, MPH
American Institutes for Research, Chicago, Illinois

Ruchi M. Fitzgerald, MD, Rush University, Chicago, Illinois

Author disclosure: No relevant financial affiliations.

Clinical Question

Do cell phone–based smoking cessation interventions increase cessation rates in people who smoke?

Evidence-Based Answer

Automated text messaging interventions are more effective than minimal smoking cessation support (absolute risk reduction [ARR] = 3%; 95% CI, 1% to 5%). (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Adding text messaging to other smoking cessation interventions is more effective than other smoking cessation interventions alone (ARR = 4%; 95% CI, 1% to 10%). (SOR: A, based on consistent, good-quality patient-oriented evidence.) When smartphone smoking cessation apps are compared with lower intensity smoking cessation support, such as printed educational materials, they have not been shown to increase the likelihood of smoking cessation.[1] (SOR: C, based on consensus, disease-oriented evidence, usual practice, expert opinion, or case series.)

Practice Pointers

In 2015, 68% of adults in the United States who smoked cigarettes reported they wanted to quit completely.[2] Cell phone interventions such as text messaging and smartphone apps are being explored as options to support smoking cessation. The potential benefits of cell phone interventions include the ease of use, cost-effective delivery and scalability to large populations, the ability to individualize and send time-sensitive messages, the opportunity to provide content that can distract from cravings, and the ability to provide social support.[1]

This Cochrane review included 26 randomized controlled trials (RCTs; N = 33,849) that compared quit rates among individuals who received text messages or smartphone app interventions vs. either a lower intensity intervention (less frequent messaging) or alternate educational interventions (such as printed cessation materials or general health information).[1] The settings, recruitment methods, and control interventions varied considerably across studies. Study settings included the United States, Canada, Europe, and Asia. Most study samples included a general adult population with similar proportions of women and men, although four focused specifically on young adults, one on pregnant patients, one on people living with HIV infection, and one primarily on military veterans. Several studies specifically included pharmacotherapy; however, in these studies pharmacotherapy was offered as standard of care with the texting and app interventions being added to support cessation efforts and, in some cases, medication adherence. Control interventions also varied considerably across studies. The primary outcome was smoking abstinence at longest follow-up, which was at least six months from baseline and was measured by self-report and/or biochemical validation.

Thirteen RCTs (n = 14,133) evaluated text messaging interventions compared with minimal smoking cessation support. The text messaging interventions included a wide range of text message styles and frequencies. Examples included automated text messaging tailored to the individual's current quit status, interactive text messaging that allowed for more support in cases of increased cravings, and a regular "check in" via text. The control groups received no or minimal smoking cessation support interventions, which also were varied. These ranged from receiving text messages that were not smoking cessation–related but pertained to general health to written materials about smoking cessation to general in-person health advice from a clinician. Moderate certainty evidence indicated that six months of text messaging was more effective than minimal smoking cessation support at achieving abstinence from smoking (ARR = 3%; 95% CI, 1% to 5%; number needed to treat = 33; 95% CI, 20 to 100).

Four RCTs (n = 997) evaluated text messaging interventions in addition to other smoking cessation support. The text messaging interventions varied in frequency and style as previously described. The smoking cessation support offered in addition to the text messaging varied across studies and included in-person smoking cessation counseling sessions and/or pharmacotherapy. Moderate certainty evidence indicated that text messaging plus other smoking cessation support was more effective than smoking cessation support alone for achieving long-term abstinence from smoking (ARR = 4%; 95% CI, 1% to 10%; number needed to treat = 25; 95% CI, 10 to 100).

Five RCTs (n = 3,079) evaluated smartphone apps that varied significantly in content and components, ranging from a positive reinforcement/behavior tracking app to supportive messages and evidence-based cessation services. The smartphone app interventions were compared with a basic app that provided general smoking cessation information or minimal non-app support such as printed educational materials about smoking cessation. There was no evidence that smartphone apps increased the rate of smoking cessation.

The U.S. Public Health Service–sponsored guideline, "Treating Tobacco Use and Dependence," recommends that physicians offer patients tobacco addiction counseling and pharmacotherapy, and include the use of telephone "quit" lines and telephone counseling for smoking cessation.[3]

The practice recommendations in this activity are available at http://www.cochrane.org/CD006611.

Editor's Note: The numbers needed to treat reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review. Dr. Salisbury-Afshar is a contributing editor for *AFP*.

References

1. Whittaker R, McRobbie H, Bullen C, et al. Mobile phone text messaging and app-based interventions for smoking cessation. *Cochrane Database Syst Rev.* 2019;(10):CD006611.
2. Babb S, Malarcher A, Schauer G, et al. Quitting smoking among adults–United States, 2000-2015. *MMWR Morb Mortal Wkly Rep.* 2017;65(52):1457-1464.
3. Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update*. U.S. Department of Health and Human Services. Public Health Service; May 2008. ■