A new progestogen-only medical therapy for outpatient management of acute, abnormal uterine bleeding: a pilot study

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OBJECTIVE: The objective of this investigation was to study short-term efficacy and feasibility of a new progestogen-only treatment for outpatient management of acute abnormal uterine bleeding.

STUDY DESIGN: This was a prospective, single-arm, pilot clinical trial of a progestogen-only bridging treatment for acute abnormal uterine bleeding in nonpregnant, premenopausal women in the Gynecologic Urgent Care Clinic at Harbor-UCLA Medical Center. Subjects were administered a depo-medroxyprogesterone acetate 150 mg intramuscular injection and given medroxyprogesterone acetate 20 mg to be taken orally every 8 hours for 3 days. The primary outcome measures included a percentage of women who stopped bleeding in 5 days, time to bleeding cessation, reduction in numbers of pads used, side effects, and patient satisfaction.

RESULTS: All 48 women stopped bleeding within 5 days; 4 women had spotting only at the time of their last contact during the 5 day follow-up. Mean time to bleeding cessation was 2.6 days. Side effects were infrequent and patient satisfaction was high.

CONCLUSION: Injection of depo-medroxyprogesterone acetate 150 mg intramuscularly combined with 3 days of oral medroxyprogesterone acetate 20 mg every 8 hours for 9 doses is an effective outpatient therapy for acute abnormal uterine bleeding.

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Background and Objective

Acute abnormal uterine bleeding (AUB), as recently reclassified, is an episode of heavy bleeding that the clinician considers sufficiently severe to require immediate intervention to prevent further blood loss. At presentation of AUB, tests are performed to determine etiology so that targeted, long-term therapy can be designed. The clinical challenge is that the bleeding needs to be halted promptly, usually before the test results are available.

No Food and Drug Administration–approved products are available for short-term treatment of acute excessive bleeding. Only 4 therapies in studies cumulatively reporting the experience of 116 women have been evaluated in prospective trials published in peer-reviewed journals. Retrospective reports add the experience of fewer than 200 more women to the literature. Many therapies used in those reports would not be used today because of safety concerns about the use of high doses of estrogen.

With high-dose oral medroxyprogesterone acetate (MPA), the median time to bleeding cessation in the best-designed randomized clinical trial was 3 days. By 3 days, serum levels of depo-medroxyprogesterone acetate (DMPA) are therapeutic. Therefore, we sought to study the ability of that combination of progestogen-only therapies to control acute AUB. We chose DMPA 150 mg given intramuscularly (IM) followed by MPA 20 mg orally every 8 hours for 9 doses.

The primary outcome measures of our pilot study included the following: (1) efficacy of the therapy in halting uterine bleeding (percentage of women who stopped bleeding, mean time to bleeding cessation, and drop in hemoglobin); (2) treatment feasibility (patient use of the study drugs as directed); and (3) tolerability (side effect reports and patient satisfaction).

Materials and Methods

Premenopausal nonpregnant women who presented with complaints of acute heavy and/or prolonged uterine bleeding were evaluated. If the patient was judged to be a candidate for outpatient care, she was invited to participate in the study. Baseline data included demographic data, information about the current bleeding episode, recent bleeding patterns, and medical problems as well as the findings from the examination and testing.

Each woman received DMPA 150 mg IM and a vial containing 18 tablets of MPA 10 mg from which she was instructed to take 2 tablets orally every 8 hours for 3 days. A formal complete blood count (CBC) was ordered before the patient left the clinic. A prescription for iron supplements was provided if she was anemic. Each patient was called on days 1 and 2 to collect the data for each of two 24-hour intervals. She returned to the clinic on day 3 to provide interval data about bleeding, pill use, and side effects and a blood sample for a repeat CBC. If a woman had not stopped bleeding by the day 3 visit, she was called on day 5 to provide data for days 4 and 5.

Results

All 48 women were premenopausal (age 19-53 years) and most were obese (mean body mass index, 34.9 kg/m^2; range, 21.5–51.2 kg/m^2). Women reported that the mean number of months of heavy (excessive) bleeding was 5.2 months. The mean duration of bleeding during their

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TABLE
Response to treatment by study day

Variable	Number of women (still) bleeding	Number of women who stopped bleeding in prior 24 hours	Cumulative number of women who stopped bleeding	Percent of women who stopped bleeding	Mean number of sanitary protection products used in prior 24 h[a]
Baseline (day 0)	48	—	—	—	8.5
Day1	36	12	12	25.0	2.0
Day2	28	8	20	42.7	1.0
Day3	14	14[b]	34	70.8	1.0
Day4	9	5	39	81.3	1.0
Day5	0	9[c]	48	100.0	0.0

[a] Number of products used by women who were still bleeding; [b] One woman was still spotting on day 3 but was lost to later follow-up; [c] Four women still had spotting but no longer required sanitary protection products.

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current episode was 30.6 days. In the 24 hours prior to presentation, women reported the use of a mean of 8.5 sanitary protection products.

No patient required either surgical intervention or additional medical treatments during the 5 day study period (Table). The mean time to bleeding cessation was 2.6 days and the median was 3 days. The amount of blood lost rapidly and significantly declined. Mean and median hemoglobin levels drawn on the day of enrollment and on study day 3 were the same.

The most common histology was proliferative endometrium (21/44), followed by secretory endometrium (7/44), sloughing endometrium (7/44), chronic endometritis (3/44), and fragments of endometrial glands and stroma (3/44). Polyps were detected in 3 cases. There were 2 cases of simple hyperplasia without atypia and 1 case of complex hyperplasia without atypia. Because all women stopped bleeding, no association was seen between histology and response to therapy. All 13 women with leiomyoma stopped bleeding.

At the end of the trial, women were asked to rate their satisfaction with the therapy using a scale of 1-3 (1, poor; 2, good; or 3, excellent). The median score was 3; the mean was 2.75. All 48 patients said they would recommend this treatment to a friend.

To address the concern that treatment with DMPA might make subsequent bleeding more difficult to treat, we conducted a quality assurance chart review. Only 15% returned within 12 weeks with complaints of subsequent spotting and/or bleeding. All responded promptly to additional medical therapy.

Comment

Although this was a single-arm, noncomparative pilot clinical trial, it is the largest prospective study to date to measure the effectiveness of a treatment of acute AUB. The most significant limitation of our pilot study is that it was not a comparative trial. Another limitation is that we studied only short-term (5 days) response to therapy. Finally, the high patient satisfaction scores could have been influenced by the experimental design.

This pilot study suggests that DMPA 150 mg IM combined with MPA 20 mg given orally 3 times a day for 3 days is an effective outpatient treatment for acute AUB among hemodynamically stable women with a variety of pathologies. It has been shown to halt bleeding rapidly, whereas appropriate testing identifies the underlying pathophysiology, thus providing a temporary bridge to long-term targeted therapies. This regimen has good compliance, few side effects, and high patient satisfaction. Future research with more organized intermediate follow-up and larger numbers of subjects could help evaluate its full potential.

CLINICAL IMPLICATIONS

- Depo-medroxyprogesterone acetate 150 mg intramuscularly combined with oral medroxyprogesterone acetate 20 mg every 8 hours for 9 doses rapidly halted acute abnormal uterine bleeding caused by a variety of benign conditions and was well accepted by patients for outpatient management. ■