Hysteroscopic Endometrial Destruction, Optimum Method for Preoperative Endometrial Preparation: A Prospective, Randomized, Multicenter Evaluation

O. Shawki, MD, A. Peters, DO, S. Abraham-Hebert, MD

ABSTRACT

Objective: To compare the outcome and cost-effectiveness of various forms of preoperative endometrial preparation prior to hysteroscopic endometrial destruction for abnormal uterine bleeding.

Methods: This was a multicenter, prospective, comparative, randomized study conducted in a tertiary care hospital in Cairo, Egypt and 2 academic tertiary care teaching hospitals in the United States. One hundred thirty-one premenopausal women, who had completed childbearing, mean age of 45.7 years, with abnormal uterine bleeding refractory to medical management without histologic evidence of endometrial neoplasia were studied. The 131 patients were randomized for preoperative preparation for hysteroscopic endometrial destruction into 1 of 5 groups as follows: Group I, dilation and curettage (D & C) (39); Group II, gonadotropin-releasing hormone analogue (GnRHa) for 1 month (23); Group III, GnRHa for 3 months (26); Group IV, danazol for 3 months (26); and Group V, medroxyprogesterone acetate (MPA) 15 mg for 3 months (27). The choice of endometrial ablation or endometrial resection was left to the surgeon.

Results: Improvement in bleeding patterns, amenorrhea, operative times, complications, and relative cost were the measured outcomes. The mean follow-up time was 1 year from the time of the procedure. Overall, in Group I, 39/39 (100%) improved and 7/39 (18.0%) experienced amenorrhea; in Group II, 21/23 (91.3%) improved and 9/23 (39.1%) experienced amenorrhea; in Group III, 24/26 (92.3%) improved and 10/26 (38.5%) experienced amenorrhea; in Group IV, 24/26 (92.3%) improved and 9/26 (34.6%) experienced amenorrhea; and in Group V, 23/27 (85.1%) improved and 7/27 (25.9%) experienced amenorrhea.

Conclusion: Endometrial destruction whether by the ablation or resection technique, regardless of the type of surgical pretreatment is a safe and effective surgical approach for treating abnormal uterine bleeding. D & C or MPA appear to be the most cost-effective pretreatment regimens. MPA pretreatment may confer the added advantage of decreasing blood flow and allowing better hysteroscopic visualization than D & C pretreatment.

Key Words: Hysteroscopy, Endometrial ablation, Abnormal uterine bleeding.

Unit of Advanced Laparoscopic Surgery, Al Ebtesama Hospital, Cairo, Egypt (Dr Shawki).

Fairground Medical Center, PA, USA (Drs Peters and Abraham-Hebert).

Address reprint requests to: Osama Shawki, MD, Al Ebtesama Hospital, 10 Aboul Magd Amer Street, 11341, Heliopolis, Cairo, Egypt. Telephone: (202) 417-00111, Fax: (202) 291-2775

INTRODUCTION

Gynecologists are called on frequently to treat menstruation disorders. When neoplastic conditions have safely been ruled out and the patient has failed medical management and has completed childbearing, hysteroscopic endometrial destruction is a viable, minimally invasive and cost-effective treatment option that can often avoid a more costly and potentially more complicated hysterectomy.[1,2] Various pretreatment regimens have been attempted to arrest endometrial growth and reduce vascularity, which are believed to enhance the success of the procedure.[3,4] With greater demands being placed on clinicians for cost-effective outcome-based treatment, it is imperative to find the most efficient regimen for treating women with this disorder.

We evaluated the outcome of operative hysteroscopic endometrial destruction in patients with abnormal uterine bleeding who were ruled out for neoplastic conditions and had failed medical management, and who were randomized to various pretreatment protocols including dilation and curettage (D & C), gonadotropin-releasing hormone analogue (GnRHa), danazol, and depot medroxyprogesterone acetate (MPA) before the operative event.

METHODS

This was a prospective, randomized, comparative investigation conducted at 3 academic teaching hospitals. One hundred thirty-one patients were enrolled in the study. The mean age of the patients was 45.7 years. All study patients had abnormal uterine bleeding refractory to medical management, underwent endometrial sampling to rule out neoplasia, and no longer desired to have children. Patients underwent thoughtful counseling with regard to future childbearing and contraceptive choices prior to enrolling in the study. Other criteria followed prior to endometrial destruction included the following: degree of abnormal uterine bleeding at a level that justified hysterectomy, uterine size < 12 weeks, and patient refusal of continued medical attempts to control bleeding.

Patients were randomized into 1 of 5 pretreatment groups before hysteroscopic endometrial destruction:

- Group I: D & C immediately before procedure.
- Group II: GnRHa, goserelin 3.6 mg SC, for 1 month before procedure.
- Group III: GnRHa, goserelin 3.6 mg SC monthly, for 3 months before procedure.
- Group IV: danazol 400-600 mg PO per day, for 3 months before procedure.
- Group V: MPA 15 mg PO per day, before procedure.

Informed consent was obtained from all patients, which explained the involved side effects, risks, and benefits of medications and the procedures. Alternative treatment options were given to patients.

All surgical procedures were performed in the ambulatory care unit, and the main outcome measures included improvement in bleeding problem, amenorrhea, operative time, complications, and relative costs.

Endometrial destruction was carried out by either the ablative technique with the 3.5-mm rollerball or by the resection technique with a 24-French cutting loop. Resection was performed with a Martin electro-diathermy unit on a blended cutting coagulation current of 70 W. The type of destruction was dependent upon the surgeon's preference; however, the surgeons were consistent with the type of technique used. We used Karl Storz hysteromat to push Glycine 1.5 fluid as a distension medium. The pressure of the apparatus is between 60 to 90 mm Hg. All procedures were carried out with a 26-French continuous flow resectoscope, fitted with a 4-mm 25-degree telescope.

Patient follow-up was for 1 year after the procedure for bleeding patterns. The patient reported the number of pad changes during menses and subjective assessment of the amount of menstrual blood loss. Complete blood count was analyzed at follow-up also.

RESULTS

The measured clinical outcomes were defined as improvement or amenorrhea. Improvement was defined as a bleeding pattern that was acceptable to the patient and clearly represented diminished menstrual flow compared with that prior to treatment. Amenorrhea was defined as no bleeding for a period $\geq$ 3 menstrual cycles.

Improvement was observed in 100% of the D & C pretreatment group, 91.3% of the GnRHa for 1 month pretreatment group, 92.3% of the GnRHa for 3 months pretreatment group, 92.3% of the danazol pretreatment group, and 85.1% of the MPA pretreatment group. No statistically significant difference existed among groups with regard to improvement status per chi-square analysis (P = 0.99) **(Table 1)**.

Amenorrhea was observed in 18% of the D & C pretreatment group, 39.1% of the GnRHa for 1 month pretreatment group, 38.5% of the GnRHa for 3 months pretreatment group, 34.6% of the danazol pretreatment group, and 25.9% of the MPA pretreatment group. No statistically significant difference existed among groups with regard to amenorrhea per chi-square analysis (P = 0.59) **(Table 1)**.

To compare the techniques of hysteroscopic endometrial resection versus ablation, the outcomes between the D & C and GnRHa for 3 months pretreatment groups was made. One hundred per cent of resection patients versus 75.8% of ablation patients experienced improvement in the D & C pretreatment group reflecting no significant difference on chi-square analysis (P = 0.79). Ninety-three percent of resection patients versus 90.9% of ablation patients experienced improvement in the GnRHa for 3 months pretreatment group showing no significant difference on chi-square analysis (P = 0.80). Amenorrhea was experienced by 30% of the resection patients undergoing D & C pretreatment versus 13.8% of ablation patients in this same group representing no significant

Table 1.
Outcome among 5 groups with various
pretreatments to endometrial destruction

Group (n)	Improvement (%)	Amenorrhea (%)
I (39)	39 (100)	7 (18)
II (23)	21 (91.3)	9 (39.1)
III (26)	24 (92.3)	10 (38.5)
IV (26)	24 (92.3)	9 (34.6)
V (17)	23 (85.1)	7 (25.9)
P-value	NS*	NS*

*comparison between any group by chi-square with Yates correction

Table 2.
Comparison of D & C and 3 months of
GnRHa prior to endometrial destruction

	Outcome			
	Improvement		Amenorrhea	
Technique	Group I	Group III	Group I	Group III
Resection	10/10 (100)	14/15 (93.3)	3/10 (30)	5/15 (33.3)
Ablation	22/29 (75.8)	10.11 (90.9)	4/29 (13.8)	5/11 (45.4)
P-value	NS*	NS*	NS*	NS†

*chi-square with Yates correction
†Fisher's exact test

difference on chi-square analysis (P = 0.63). Amenorrhea was experienced by 33.3% of GnRHa for 3 months pretreatment who underwent resection versus 45.4% of this group undergoing ablation with no significant difference shown with Fisher's exact test (P = 0.48) **(Table 2)**.

Associated operative factors including operative time, complications and relative costs among the various pretreatment groups were also studied. Operative times were 68 ± 7, 39 ± 7, 37 ± 5, 43 ± 3, and 54 ± 9 minutes for the D & C, GnRHa for 1 month, GnRHa for 3 months, danazol, and MPA pretreatment groups, respectively. Operative times were significantly longer for the D & C and MPA groups compared with that of the other groups, but were not significantly different from each other on analysis of variance with the Ducan multiple range test, P < 0.05. The only complication among our patients was 1 case of fluid overload that was successfully and easily treated with diuretics and observation. The cost of the various pretreatments (excluding procedure fees) in decreasing order was GnRHa for 3 months which is greater than the cost of danazol for 3 months which is greater than the cost of GnRHa for 1 month which is greater than the cost of MPA which is greater than the cost of D & C pretreatment groups.

CONCLUSION

Endometrial ablation-resection is a safe and effective means of controlling abnormal uterine bleeding (AUB) refractory to medical management.[5-7] This study demonstrates many points of interest that can facilitate clinical decision-making in the surgical management of AUB refractory to medical management. At a time when cost-effectiveness of surgical procedures is paramount, it is imperative to scrutinize treatment outcomes, cost, operative times, and complications to select the most appropriate and efficacious management for patients.

The overall premise of this study shows no significant difference with regard to improvement or amenorrhea based on various pretreatments prior to endometrial destruction including D & C, GnRHa, danazol, or MPA. This is consistent with the findings of Seeras and Gilliland,[8] who reported a trend but not a significant difference between the preoperative use of GnRHa or danazol, and between ablation versus resection of the endometrium.[8] Maia et al[9] achieved amenorrhea in 50% of patients with no preoperative pretreatment before endometrial resection in a series of 70 patients with menorrhagia. Conversely, however Sorensen et al[10] found an increased rate of amenorrhea at 1 year in the GnRHa pretreatment group compared with no pretreatment for endometrial resection. Fraser et al[11] compared GnRHa and danazol before endometrial ablation and showed a similar effect with 74% of GnRHa users and 62% of danazol users achieving amenorrhea after 6 months of follow-up. The strength of our study is based on the comparison of a wide array of hysteroscopic pretreatment.

For the purpose of the study, improvement included both diminished menstrual flow and amenorrhea over the measured follow-up period of 1 year. Our patients achieved excellent improvement rates of 85.1% to 92.3% regardless of the type of pretreatment used. These results are consistent with the results reported by others.[12]

Although the rate of amenorrhea in our study was relatively low (18% to 39.1%) when compared with that in other studies (50% to 74%), our follow-up interval was measured up to 1 year after surgery, whereas the studies demonstrating higher rates of amenorrhea were followed for the considerably less time of 2 to 6 months.[9,11] We and others believe that longer follow-up periods may yield greater recurrence rates of bleeding, which may require reoperation.[12]

We found no statistically significant difference in the outcome after endometrial resection versus ablation **(Table 2)**. Others have reported similar rates when resection or ablation techniques are used.[8] The similar outcomes demonstrated by resection and ablation suggest that the surgeon should use the technique that best fits his or her training and skill.

Operative times were measurably longer in the D & C and MPA pretreatment groups compared with those in the GnRHa and danazol groups. In the case of D & C pretreatment, the added time is accounted for by the time required to set up and perform the D & C procedure prior to endometrial destruction. The MPA pretreatment group also required a longer time due to greater endometrial thickness in some patients requiring repetitive destruction and instrument cleaning. Operative times were consistent with times reported by others **(Table 3)**.[10]

Complications were fortunately rare in our study. Only 1 case of fluid overload was experienced, and it was easily dealt with through diuresis and observation.

Cost is an important factor in any treatment. Cost analysis must also demonstrate acceptable quality for the treatment in question. Although reduced hospital costs and shorter recovery periods have been realized by using endometrial destructive techniques versus hysterectomy, definitive treatment of AUB favors hysterectomy. Among the hysteroscopic endometrial destruction groups, various pretreatments will greatly affect the overall cost. The most costly pretreatments included the use of GnRHa for 3 months prior to the surgical procedure followed by danazol pretreatment for 3 months, GnRHa for 1 month, D & C, and MPA.

In conclusion, endometrial destruction whether performed with the ablation or resection technique is a safe, effective means to surgically control AUB.[5] Surgeon preference should dictate which procedure is used. Our study demonstrated no significant difference in outcome regardless of

Table 3.
Associated operative factors.

Group	Operative Time (min)	Complications	Relative Costs*
I	68 ± 7†	1‡	$
II	39 ± 7	0	$$$
III	37 ± 5	0	$$$$$$
IV	43 ± 3	0	$$$$
V	54 ± 9†	0	$$

*not including procedure fee.
†significantly different from other groups by analysis of variance with Duncan multiple range test.
‡fluid overload.

the type of pretreatment used. In this regard, the authors recommend the most cost-effective pretreatment prior to the surgical procedure, which includes either D & C or MPA for 3 months Medroxyprogesterone acetate confers the added advantage of controlling bleeding and induction of an endometrial atrophying effect on the endometrium, thus giving the surgeon better visualization for the procedure.

References:

1. Neuwirth RS, Duran AA, Singer A. The endometrial ablator. *Obstet Gynecol*. 1994;83:792-796.

2. DeCherney AH, Polan ML. Hysteroscopic management of intrauterine lesion and intractable bleeding. *Obstet Gynecol*. 1983;61:392-397.

3. Serden PS, Brooks PG. Preoperative therapy in preparation for endometrial ablation. *J Reprod Med*. 1992;37:679-681.

4. Valle RF. Endometrial ablation for dysfunctional uterine bleeding: role of GnRH agonist. *Int J Gyn Obstet*. 1993;41:3-15.

5. Vilos GA, Vilos EC, King JH. Experience with 800 hysteroscopic endometrial ablations. *J Am Assoc Gynecol Laparosc*. 1996;4:33-38.

6. Tapper AM and Heinonen PK. Hysteroscopic endomyometrial resection for the treatment of menorrhagia: follow-up of 86 cases. *Eur J Obstet Gynecol Reprod Biol*. 1995;62:75-79.

7. Paskowitz RA. "Rollerball" ablation of the endometrium. *J Reprod Med*. 1995;40:333-336.

8. Seeras RC, Gilliland GB. Resumption of menstruation after amenorrhea in women treated by endometrial ablation and

myometrial resection. *J Am Assoc Gynecol Laparosc*. 1997;4:305-309.

9.   Maia H Jr., Calmon LC, Marques D, Coutinho EM. Administration of medroxyprogesterone acetate after endomyometrial resection. *J Am Assoc Gynecol Laparosc*. 1997;4:195-200.

10.   Sorensen SS, Colov NP, Vejerslev LO. Pre- and postoperative therapy with GnRH agonist for endometrial resection. A prospective, randomized study. *Acta Obstet Gynecol Scand*. 1997;76:340-344.

11.   Fraser IS, Healy DL, Torode H, Song JY, Mamers P, Wilde F. Depot goserelin and danazol pretreatment before rollerball endometrial ablation for menorrhagia. *Obstet Gynecol*. 1996;87:544-550.

12.   Steffensen AJ, Schuster M. Endometrial resection and late reoperation in the treatment of menorrhagia. *J Am Assoc Gynecol Laparosc*. 1997;4:325-329.