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Novasure as a Mechanical Endometrial Preparation Agent in Large Uteri

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ABSTRACT

Objective: We evaluated Novasure ablation as a mechanical endometrial preparation agent before Roller Ball endometrial ablation in lieu of GnRH agonists in large uteri.

Methods: A retrospective chart review of 20 consecutive patients undergoing Novasure ablation for mechanical endometrial preparation before Roller Ball ablation (RB-Novasure group) was conducted and the results compared to that of 23 consecutive patients who received GnRH agonist (Leuprolide acetate) as a medical endometrial preparation before Roller Ball ablation (RB-Lupron group). The postoperative follow-up time frame was divided into immediate (3 mo), intermediate (3 to 12 mo) and long-term (12 to 32 mo). Rates of amenorrhea, heavy bleeding, cramping, and failure (repeat ablation or hysterectomy for heavy bleeding or persistent pain) were compared between the 2 groups.

Results: The mean rates of amenorrhea for the patients not lost to follow-up at 3 mo, 3 to 12 mo, and 12 to 32 mo visits were 45.5%, 58.8%, and 44.4% for the RB-Lupron group, and 80%, 86.7%, and 100% for the RB-Novasure group ($P = .02$, $P = .08$, and $P = .02$). Failure rates were 4.8%, 6.2%, and 55.6% for the RB-Lupron group; and 0 (0/20), 12.5% (2/16) and 0 (0/8) for the RB-Novasure group ($P = .51$, $P = .50$, and $P = .02$). The RB-Novasure group had a significantly lower rate of heavy bleeding and cramping. 86.4%, 58.8%, and 33.3% patients reported satisfaction with their treatment in the RB-Lupron group and 100%, 87.5%, and 75% in RB-Novasure group ($P = .13$, $P = .07$, and $P = .11$).

Conclusion: Novasure ablation, for mechanical endometrial preparation before Roller Ball ablation, appears to be a superior alternative to medical preparation with GnRH agonists in patients with large uteri.

Key Words: Endometrial ablation, GnRH agonist, Menorrhagia, Novasure, Roller Ball.

INTRODUCTION

Menorrhagia is a major cause of morbidity among women. Although various definitions for menorrhagia exist with varying degrees of blood loss (60cc to 80cc) per menstruation, recent recommendations suggest that menorrhagia should be defined as "excessive menstrual blood loss, which interferes with the woman's physical, emotional, social, and material quality of life, and which can occur alone or in combination with other symptoms."[1] Worldwide, there are approximately 19% of women of reproductive age suffering from menorrhagia.[2] It is the most common reason for gynecologic office visits in the United States.[3] For women refractory to medical treatment for menorrhagia, endometrial ablation is an alternative to hysterectomy. Studies have shown that endometrial ablation, compared to hysterectomy, is associated with faster patient recovery, shorter hospital stay, earlier return to work, fewer complications, and reduced costs.[4-6]

A recent Cochrane review concluded that success rates and complication profiles of newer nonhysteroscopic global ablation techniques involving heated fluid, thermal balloon, radio frequency, microwave energy, or cryotherapy compared favorably with first-generation transcervical hysteroscopic methods, such as resection and ablation procedures (laser, loop resection, Roller Ball cautery).[7] However, in our clinical experience, nonhysteroscopic devices alone had a higher failure rate with larger uteri (not enough area ablated) and fibroid uteri (distorting the cavity and limiting the ablation). In these cases, the only option, other than hysterectomy, is to resort back to transcervical hysteroscopic ablation. In this process, most hys-

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teroscopic ablative procedures, like Roller Ball, are able to destroy 4 mm to 6 mm of the endometrium and preoperative endometrial preparation before ablation aids by making the endometrial lining thinner. A Cochrane review of preoperative endometrial thinning agents, prior to an ablative procedure, showed GnRH agonists to be superior to both danazol and progesterone.[8] However, medical endometrial preparation, particularly with GnRH analogs, is associated with adverse effects, considerable wait period prior to ablation, and significant cost.

We therefore resorted to performing mechanical endometrial preparation as an alternative to medical endometrial preparation. Since simple curettage of the endometrium leads to visualization problems for the subsequent hysteroscopic ablation, we evaluated Novasure as a means of mechanical endometrial preparation before Roller-Ball endometrial ablation in place of GnRH agonists.

MATERIALS AND METHODS

We reviewed the charts of 20 consecutive patients who underwent Novasure ablation as mechanical endometrial preparation before Roller Ball ablation (RB-Novasure group) performed by a single surgeon. We also reviewed the charts of 23 consecutive patients who received GnRH agonist (Leuprolide acetate) as medical endometrial preparation before Roller Ball ablation performed by the same surgeon (RB-Lupron group). The RB-Lupron group served as the control group. This pilot study was conducted at Temple University Hospital at Philadelphia after obtaining Institutional Review Board approval. All patients had large uteri, defined as uterine volume > 200cc,[3,9] normal Papanicolaou test within the past year, and normal preoperative endometrial biopsy. Demographic data, indication for ablation, postoperative symptoms, and information about whether the patient had reablation or hysterectomy were collected.

Patients undergoing medical preparation of the endometrium received a single dose of Leuprolide acetate (Lupron) 11.25 mg approximately 1 to 3 mo before the scheduled ablation with Roller Ball. The mechanical preparation group underwent Novasure, followed by Roller Ball ablation of the endometrium in the same sitting. Roller Ball ablation in both groups was performed in standard fashion, by using 1.5% glycine as the distention medium and electrocautery set at 100 cutting and 100 coagulation.

The postoperative follow-up time frame was divided into immediate (3 mo), intermediate (3 to 12 mo), and long-term (12 to 32 mo) groups. A survey was also mailed to all the patients regarding their postoperative symptoms. Amenorrhea was defined as the complete absence of bleeding, and "heavy bleeding" as bleeding heavier than that before surgery. Cramping was defined as lower abdominal or pelvic pain affecting the activities of daily living. The patient was also asked to comment on whether she was satisfied or not with the treatment. Failure of the procedure was considered if the patient underwent a repeat ablation or hysterectomy for heavy bleeding or persistent pain. Data were entered into an Excel spreadsheet (MS Excel, Microsoft, Richmond USA) and analyzed using SPSS (SPSS Inc, Version 16 for Mac OS X).

RESULTS

A total of 43 patients were included in the study. Twenty-three (53.5%) underwent Roller Ball ablation with Leuprolide acetate endometrial preparation (RB-Lupron), and 20 (46.5%) patients underwent Roller Ball ablation with Novasure endometrial preparation (RB-Novasure). The baseline characteristics of the cohort are described in the **Table 1**. A comparison of means established that both the groups were comparable. The reasons for large uteri in both groups are described in **Table 2**.

The rate of follow-up at 3, 3 to 12 and 12 to 32 mo was 100%, 77% and 41% for the RB-Lupron group and 100%, 75%, and 40% for the RB-Novasure group. The results of amenorrhea, heavy bleeding, cramping or pelvic pain, satisfaction and failure rates for both groups are summarized in **Table 3**. The group with Novasure as an endometrial preparatory agent (RB-Novasure) showed a significantly higher amenorrhea rate at 3, 3 to 12, and 12 to 32 mo intervals. For the patients not lost to follow-up, the mean rates of amenorrhea were 45.5%, 58.8%, and 44.4%, respectively, for the RB-Lupron group, and 80%, 86.7%, and 100% for the RB-Novasure group ($P = .02$, $P = .08$, and $P = .02$) **(Figure 1)**. The RB-Novasure group also had a lower rate of heavy bleeding and significantly lower cramping or pelvic pain at all 3 time intervals **(Table 3)**. Patient-reported satisfaction rates at all 3 time-intervals were 86.4%, 58.8%, and 33.3% for the RB-Lupron group, and 100%, 87.5%, and 75% with the RB-Novasure group ($P = .13$, $P = .07$, and $P = .11$) **(Figure 2)**. Failure rates (defined as repeat ablative procedure or hysterectomy for heavy bleeding or persistent pain) were 4.8%, 6.2%, and 55.6% for the RB-Lupron group; and 0 (0/20), 12.5% (2/16), and 0 (0/8) for the RB-Novasure group ($P = .51$, $P = .50$ and $P = .02$) at 3, 3 to 12, and 12 to 32 mo intervals, respectively **(Figure 3)**.

Table 1.
Mean Baseline Characteristics of the 2 Groups

Variable	RB-Lupron [Mean (SD)][a]	RB-Novasure [Mean (SD)][a]	Significance (P)
Age (Years)	41.57 (±4.93)	43.45 (±6.52)	.29
Gravida	3.61 (±1.65)	2.68 (±1.64)	.08
Parity	2.74 (±1.42)	2.05 (±1.27)	.11
BMI[a] (kg/m^2)	31.91 (±5.44)	31.44 (±9.49)	.85
Uterine Volume (mL)	396.18 (±152.76)	514.92 (±288.86)	.35
Length of Procedure (mins)	42.65 (±13.861)	47.94 (±25.78)	.46
Maximum follow-up Duration (days)	323.69 (±281.53)	277.44 (±214.77)	.55

[a]RB-Lupron=GnRH agonists as medical endometrial preparation before Roller Ball ablation. RB-Novasure=Novasure ablation as mechanical endometrial preparation before Roller Ball ablation; SD=Standard Deviation; BMI=Body Mass Index.

Table 2.
Reasons for Large Uteri in the 2 Groups

	RB-Lupron[a]	RB-Novasure[a]	P Value
Fibroids	7/23 (30.4%)	8/20 (40%)	.37
Adenomyosis	2/23 (8.7%)	1/20 (5%)	.55
General Uterine Enlargement[b]	0/23 (0%)	2/20 (10%)	.21

[a]RB-Lupron=GnRH agonists as medical endometrial preparation before Roller Ball ablation; RB-Novasure=Novasure ablation as mechanical endometrial preparation before Roller Ball ablation

[b]Uterine enlargement not due to fibroids or adenomyosis.

There was 1 uterine perforation, 1 difficult extubation in the RB-Lupron group, and 2 cases of false passage (defined as partial entry of dilator into the myometrium) in the RB-Novasure group.

DISCUSSION

This study presents a novel concept of using Novasure for endometrial preparation before Roller Ball ablation. In patients with large uteri, Novasure, as a mechanical method of endometrial preparation, appears to be more effective than medical endometrial preparation with Leuprolide acetate before Roller Ball ablation. Overall, the RB-Novasure group had higher rates of persistent amenorrhea, lesser rates of heavy bleeding, cramping, pelvic pain, and failure. Patients in the RB-Novasure group also reported higher satisfaction, compared to the RB-Lupron group.

Novasure, as a mechanical endometrial preparation agent, thus has several advantages over the GnRH agonists. When mechanical endometrial preparation is done with Novasure, Roller Ball ablation can be scheduled sooner, without a typical delay of 30 d to 90 d involved with medical endometrial preparation. Although our study did not address the issue of side effects, the typically reported side effects of GnRH agonist (Leuprolide acetate), such as headache, depression, insomnia, fatigue, dizziness/vertigo, skin reaction, hot flashes, decreased libido, nausea/vomiting, altered bowel function, weight gain/loss, vaginitis, and urinary symptoms[10] can be eliminated when Novasure is used.

Novasure, in addition to Roller Ball, increased the overall mean operative time by only 5 min; hence, it did not significantly increase operating room costs. Also, the cost of a Novasure is $600 per device, which is significantly lower than the cost of the GnRH agonist (Leuprolide acetate)[11] of $2,073 dollars per dose.

In the subset of women with larger uteri and uterine fibroids, Novasure alone is associated with higher failure rate.[12-14] In the current study, this drawback was overcome by hysteroscopic guidance during the actual treatment with Roller Ball. Using hysteroscopic Roller Ball endometrial ablation as a definitive treatment also ensures that trainees at teaching institutions will still have the opportunity to learn the skill of Roller Ball ablation. A single gynecologist performed all of these cases of Roller Ball ablation in this study, removing operator bias with respect to surgical technique.

Some of the limitations of this study include its retrospective nature, the nonrandomized allocation of patients, a relatively short duration of follow-up, the loss of follow-up on half the patients by 32 mo, and the potential for an increased depth of desiccation when 2 endometrial ablation techniques are used together. A

Table 3.
Symptoms Evaluated Over the 3 Time Frames for the 2 Groups

Variable	Follow-up	RB-Lupron (%)[a]	RB-Novasure (%)[a]	P Value
Amenorrhea	3 months	10/22 (45.5)	16/20 (80)	.02
	3-12 months	10/17 (58.8)	13/15 (86.7)	.08
	12-32 months	4/9 (44.4)	8/8 (100)	.02
Heavy bleeding	3 months	2/22 (9.1)	0/20 (0)	.27
	3-12 months	3/17 (17.6)	0/15 (0)	.14
	12-32 months	3/9 (33.3)	0/5 (0)	.20
Cramps/Pelvic pain	3 months	6/22 (27.3)	0/20 (0)	.01
	3-12 months	6/17 (35.3)	0/15 (0)	.02
	12-32 months	7/9 (77.8)	1/7 (12.5)	.01
Satisfaction	3 months	19/22 (86.4)	20/20 (100)	.13
	3-12 months	10/17 (58.8)	14/16 (87.5)	.07
	12-32 months	3/9 (33.3)	6/8 (75)	.11
Failure (repeat ablation or hysterectomy)	3 months	1/21 (4.8)	0/20 (0)	.51
	3-12 months	1/16 (6.2)	2/16 (12.5)	.50
	12-32 months	5/9 (55.6)	0/8 (0)	.02

[a]RB-Lupron=GnRH agonists as medical endometrial preparation before Roller Ball ablation. RB-Novasure=Novasure ablation as mechanical endometrial preparation before Roller Ball ablation.

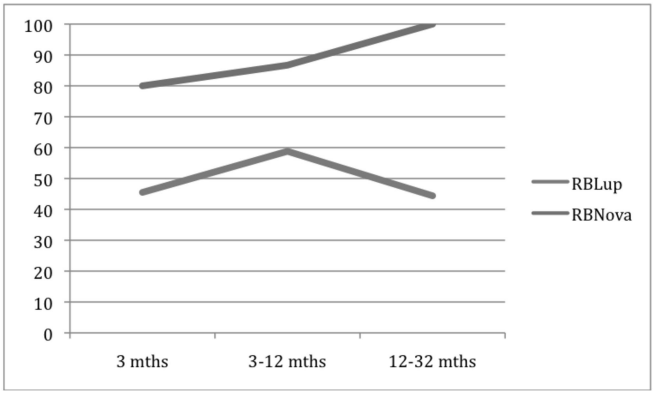

Figure 1. Rate of amenorrhea in 2 groups.

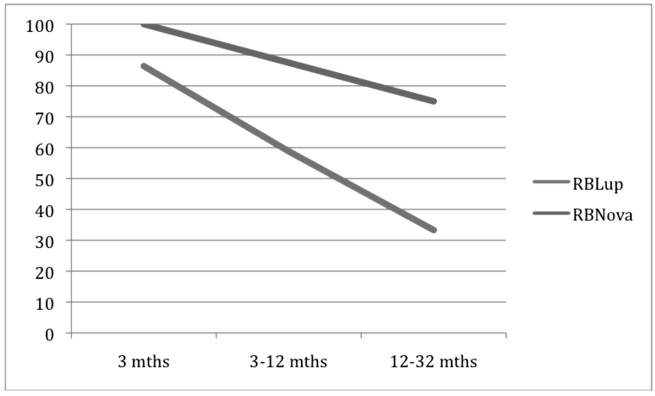

Figure 2. Satisfactory result postablation in 2 groups.

single operator performed all of the cases of Roller Ball ablation, increasing the precision, but reducing the generalizability, of the findings. Nevertheless, this pilot study provides important proof of the concept and aids in designing a prospective study. A larger sample size, and the participation of multiple operators to perform the procedures will help overcome the limitation of low generalizability of the study. We also recommend a collection of quality of life scores prospectively to better define patient satisfaction.

CONCLUSION

Our pilot study shows that the combination of both Novasure and Roller Ball ablation seems to be more effective than preparation with GnRH agonist (Leuprolide acetate) before Roller Ball ablation in terms of achieving persistent amenorrhea, and significantly lower cramping or pelvic pain in patients with large uteri. Also, the mean failure rate (repeat ablation or hysterectomy for heavy bleeding or persistent pain), although not statistically significant, showed a trend towards a gradual, long-term higher fail-

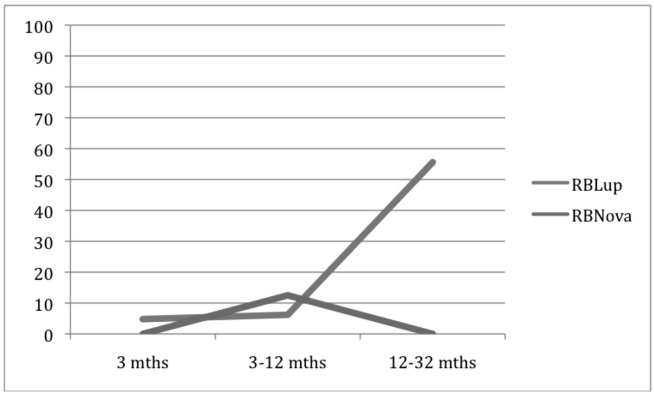

Figure 3. Rate of failure in 2 groups.

ure rate for the RB-Lupron group, compared to the RB-Novasure group **(Figure 3)**.

To our knowledge, this is the first report of 2 endometrial ablation techniques, from first and second-generations, used in tandem to achieve a greater success rate. Although the number of patients in each group is small, we did get statistically significantly higher amenorrhea rates and lower long-term failure rates with this combination. This is only a pilot study, and it is not the current standard of care to perform 2 endometrial ablation techniques together. Further prospective studies are needed to evaluate the effectiveness of Novasure as a method of endometrial preparation prior to Roller Ball ablation.

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