OBJECTIVE: To compare the effectiveness of two second-generation ablation techniques, bipolar radiofrequency impedance-controlled endometrial ablation and hydrothermablation, in the treatment of menorrhagia.

METHODS: This study was a double-blind, randomized controlled trial, which took place in a large teaching hospital in The Netherlands with 500 beds. Women with menorrhagia were randomly allocated to bipolar radiofrequency ablation (bipolar group) and hydrothermablation (hydrotherm group). At follow-up, both women and observers remained unaware of the type of treatment that had been performed. The primary outcome was amenorrhea. Secondary outcome measures were patient satisfaction and reintervention.

RESULTS: We included 160 women in the study, of which 82 were allocated to the bipolar group and 78 to the hydrotherm group. No complications occurred in either of the treatment groups. After 12 months, 87% (65 of 75) of the patients in the bipolar group were completely satisfied with the result of the treatment compared with 68% (48 of 71) in the hydrotherm group (relative risk 1.3, 95% confidence interval [CI] 1.03–1.6). The amenorrhea rates were 47% (35 of 75) in the bipolar group and 24% (17 of 71) in the hydrotherm group (relative risk 2.0, 95% CI 1.2–3.1). The relative risks for a reintervention in the bipolar group compared with the hydrotherm group was 0.29 (95% CI 0.12–0.67), whereas for hysterectomy, this was 0.49 (95% CI 0.15–1.5).

CONCLUSION: In the treatment of menorrhagia, bipolar radiofrequency endometrial ablation system is superior to hydrothermablation.

CLINICAL TRIAL REGISTRATION: ISRCTN Register, www.isrctn.org, ISRCTN23845359.

LEVEL OF EVIDENCE: I

Excessive menstrual bleeding, or menorrhagia, is a frequent problem in women of reproductive age. The definition of menorrhagia is menstrual blood loss exceeding 80 mL from normal secretory endometrium. Its incidence varies between 9% and 14%. The disorder may cause iron deficiency anemia but also shows significant effects on the medical, socioeconomic, and psychologic well-being of women. Approximately 30–40% of hysterectomies are performed for treatment of severe dysfunctional bleeding.

Endometrial ablation is an alternative to hysterectomy in women with dysfunctional bleeding. The first-generation devices for ablation were endometrial laser ablation, transcervical resection of the endometrium, and rollerball ablation. These techniques had disadvantages such as fluid overload or water intoxication. Second-generation techniques overcome these disadvantages of the first-generation techniques. Moreover, these techniques require less skill of the surgeon.
The NovaSure endometrial ablation device (bipolar radiofrequency endometrial ablation) is one of the second-generation devices that use bipolar, radiofrequency, impedance-controlled endometrial ablation to evaporate endometrial tissue. Recently, bipolar radiofrequency endometrial ablation was reported to be superior over balloon ablation, making it the standard of choice in women requesting ablation for dysfunctional uterine bleeding. However, the method also has disadvantages. It is a blind procedure, which is performed without hysteroscopic view. The size and shape of the uterus must be fairly normal to use the system, and intracavitary leiomyomas or large polyps interfere with the placement of the device.

The HydroThermAblator (hydrotherm endometrial ablation) system is a second-generation technique that is applied under hysteroscopic view, thus potentially reducing the risk of uterine perforation. In a randomized multicenter study, hydrothermablination was found to be equally effective as rollerball ablation. Randomized comparisons between bipolar radiofrequency and hydrotherm endometrial ablation are lacking. In view of this lack of knowledge, we performed a randomized controlled trial comparing these two second-generation endometrial devices in women with menorrhagia.

MATERIALS AND METHODS

We performed a randomized controlled trial in the Máxima Medical Centre, Veldhoven, The Netherlands. The Máxima Medical Centre is a teaching hospital with 500 beds in the south of The Netherlands. The study was approved by the Institutional Review Board (No. 457). All participants provided written informed consent before enrollment.

Women with menorrhagia were eligible for the trial. Menorrhagia was defined as indicated on the pictorial chart described by Higham et al. During their period, the patient records the use of tampons and towels and the loss of clots on a scoring system. A lightly stained towel or tampon scored 1 point, a moderately stained towel or tampon 5 points, and a towel or tampon that was saturated with blood scored 20 points. A clot the size of one p scored 1 point, a 50-p-sized clot scored 5 points, and flooding also scored 5 points. One period is counted and a minimum score of 150 points was described as menorrhagia.

We did not select the patients with anemia because women in The Netherlands are seen by their general practitioner first. Most of them were already treated with iron therapy and would not have low hemoglobin or hematocrit in the hospital.

Saline infusion sonography or diagnostic hysteroscopy was required to confirm a normal uterine cavity, with a cavity length of 6–12 cm and a histologically benign endometrium.

All women underwent sonography. Patients with minimal intracavitary pathology such as type 2 fibromas and small polyps (both 2 cm or less) were also included. All women had to have a normal Pap test result, a negative Chlamydia test of the cervix, and a premenopausal follicular stimulating hormone level of less than 40 international units/L. Exclusion criteria were the presence of coagulopathies, use of anticoagulants, a desire to preserve fertility, prior uterine surgery (except low segment cesarean delivery), and suspected or confirmed uterine malignancy. All women who were included in the study preferred to be treated by endometrial ablation after careful evaluation of the advantages and disadvantages of the other treatment options.

We planned surgery in day 3–8 of the menstrual cycle. Both groups received no medical endometrial pretreatment before surgery because of the side effects of the medication and the bipolar group would have been treated unnecessarily. All patients had 250 mg naproxen 12 hours and 1 hour before treatment. Computer-generated randomization was performed by one of the authors (J.P. or R.E.) just before the start of treatment in a 1:1 ratio.

Patients and investigating doctors were masked for the randomization allocation and remained so during the study. The doctors performing the endometrial ablation did know at that moment which device was used. The patient did not know. The physician who saw the patient at the follow-up visits did not know which device was used. At the 12-month follow-up visit, the patient was told which device was used for the endometrial ablation. The ablation treatments in both arms were all performed by two gynecologists (C.K. or M.B.) specialized in these ablation techniques. Both surgeons had equal experience with each device.

The bipolar radiofrequency endometrial ablation system consists of a generator and a disposable device. When suction is applied, the endometrial lining is brought into contact with the electrode array. It is suitable for a uterus with a minimum of 2.5-cm cornu-to-cornu distance and a depth of 6–11 cm as measured by uterine sounding.

The hydrothermablination provides controlled endometrial ablation by circulating heated saline in the uterine cavity under hysteroscopic vision. The disposable sheath is inserted into the uterine cavity under...
direct hysteroscopic vision. A tight seal is necessary to prevent leakage of heated saline through the cervix.

First a diagnostic hysteroscopy with room-temperature saline was performed to rule out intracavitary pathology. Continuous-flow circulation is maintained by gravity inflow and an aspiration pump. The fluid pressure is determined by the height of the fluid measurement reservoir and saline bag. The height of the reservoir is 115 cm above the patient’s uterus; it gives a net pressure of saline into the uterine cavity of 50–55 mmHg, which is well below the 70 mmHg at which the tubes are opened. Once the diagnostic hysteroscopy was finished, the ablation treatment was started. The ablating phase starts with heating the saline in the heating canister; the temperature is displayed on the panel. It takes approximately 3 minutes to heat the saline to 90°. The ablation cycle takes 10 minutes; the timer is set on the display. During the heating and treatment cycle, the procedure automatically stops when the fluid loss is 10 mL.

We measured the duration of the procedure, which was defined as the moment the gynecologist started with introduction of a speculum until the end of the ablation. Patients in both groups were treated in a day-care program using either spinal or general anesthesia. Follow-up visits were carried out at the outpatient clinic at 4 weeks, 6 months, and 12 months after the initial treatment. At these consultations, the patients were seen by a doctor who was unaware of the treatment that had been performed. At each visit, duration of menstruation, presence of dysmenorrhea, and clots were registered. Patients also completed a pictorial chart and expressed their satisfaction about the treatment result. Level of satisfaction was categorized as completely satisfied, satisfied, doubtful, or not satisfied. Furthermore, we registered whether a reintervention had been performed. Reinterventions considered were the use of oral contraceptives and performed hysterectomies. Menstrual bleeding was quantified using the Pictoral Blood Loss Assessment Chart of Higham et al. A score of zero operationally defined “amenorrhea.”

The primary outcome measure was amenorrhea at 12 months posttreatment. Secondary outcome measures were the reduction in bleeding, patient satisfaction, and complications and hysterectomies in both groups.

We anticipated an amenorrhea rate of 30% in the hydrotherm group.14 Using an equivalence assumption with a 90% success rate for both groups and an acceptable difference of at maximum 15%, we needed 72 women per arm (80% power).17 Assuming that approximately 90% of enrolled patients would complete the study protocol, a total of 160 patients (hydrotherm:bipolar 1:1) had to be enrolled.

The analysis was performed according to the “intention-to-treat” principle, ie, patients were analyzed in the group to which they had been allocated. Patients in whom a hysterectomy was performed for bleeding complaints were considered as being amenorrheic.

Repeated-measures analysis of variance was used to evaluate changes in effect over time (time effect), differences in effect between both treatment groups (treatment effect), and interaction between changes in effect over time and treatment group (time-by-treatment effect).18 Patients with missing measurements were included in the repeated measure analysis if data were available for at least two different time points.19 P values <.05 were considered to indicate statistically significant differences. When a statistically significant difference in menstrual pattern and patient satisfaction between both treatment groups or an interaction between changes in menstrual pattern and patient satisfaction over time and treatment group was found, the differences between treatment groups at specific points in time were examined. In case of dichotomous end points, this was done by calculating relative risks and 95% confidence intervals (CIs). For the continuous outcome duration of menstruation, we calculated a difference of the medians with a 95% CI using a bootstrap procedure.20 The pictorial chart scores were compared using the Wilcoxon test.21

RESULTS

Between March 21, 2005, and August 30, 2007, 160 women were included in the study, of which 82 patients were allocated to the bipolar endometrial ablation group and 78 patients to the hydrothermablation group (Fig. 1). The baseline characteristics of both groups were comparable (Table 1).

All women included in the study underwent sonography. Furthermore, 59 women in the hydrotherm group and 58 women in the bipolar group had a saline infusion sonography, and in each group, 17 patients underwent a hysteroscopy.

Three patients (one in the hydrotherm group and two in the bipolar group) decided not to undergo the endometrial ablation after randomization, because they became frightened of the procedure. Three patients in the hydrotherm group underwent bipolar radiofrequency endometrial ablation because of technical problems with the hydrothermablation device in the operating room at the moment the treatment had to be performed.

The average duration of the bipolar group was 11.8 minutes (range 5–40 minutes) compared with 27.8 minutes (range 14–55 minutes) for the hydro-
thermablation group \((P<.001)\). In the bipolar group, one patient had a perforated uterus. In three patients in the hydrothermablation group, leakage of saline was reported, but it was possible to complete the procedure in these three patients. Two of these three women reported to be satisfied with the treatment result at 12 months.

Overall, seven patients in each group were lost to follow-up after 12 months (Fig. 1). Baseline characteristics of the patients lost to follow-up were comparable to those included in the study, but numbers were too low to compare this for statistical significance (Table 1). Figure 2 shows the patient satisfaction at 4 weeks and at 6 and 12 months after treatment. Both treatment and time effect of patient satisfaction were statistically significant \((P<.001)\), whereas time-by-treatment effect showed no significant interaction \((P=.06)\). At 12 months, the patients were more satisfied after bipolar endometrial ablation \((\text{relative risk} 1.3, 95\% \text{ CI} 1.0–1.6)\).

Figure 3 shows the percentage of women with amenorrhea, absence of dysmenorrhoea, and absence of clots after bipolar endometrial ablation and hydrothermablation. There were significantly more women reporting amenorrhea at 6 and 12 months after the procedure in the bipolar group \((\text{relative risk}

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Fig. 1. Trial profile.

at 12 months 2.0, 95% CI 1.2–3.1). A sensitivity analysis showed that when all women who were lost to follow-up after bipolar radiofrequency endometrial ablation would have had amenorrhea, the relative risk at 12 months would have been 2.1 (95% CI 1.3–3.3). In contrast, when all women that were lost to follow-up after hydrothermablation would have had amenorrhea, the relative risk at 12 months would have been 1.7 (95% CI 1.1–2.7).

There was a significant decrease in duration of menstruation after 6 and 12 months in both groups as compared with the duration of menstruation at baseline (P < .001). The duration of menstruation was significantly shorter in the bipolar group in time, treatment, and time-by-treatment effect (P < .001). Figure 4 shows the median pictorial chart score in both groups at baseline, 4 weeks, 6 months, and 12 months after the procedure.

Six months after the procedure, 24 reinterventions had been performed in total, five in the bipolar group compared with 19 in the hydrotherm group. One patient in the bipolar group had bipolar endometrial ablation again, whereas four women had a hysterectomy. In the hydrotherm group, eight patients underwent a bipolar endometrial ablation procedure, three patients started oral contraceptives, and eight women underwent a hysterectomy.

At 12 months, only two more reinterventions were performed. One patient started oral contraceptives in the bipolar group and one patient underwent bipolar endometrial ablation in the hydrothermablation group. All reinterventions were performed because of persisting menorrhagia. Pathologic examination showed normal-sized uteri in all cases. At 12 months, six reinterventions had been performed in the bipolar group compared with 20 in the hydro-

**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Bipolar Group (n=82)</th>
<th>Hydrotherm Group (n=78)</th>
<th>Bipolar Group (n=7)</th>
<th>Hydrotherm Group (n=7)</th>
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</thead>
<tbody>
<tr>
<td>Age (y)</td>
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<td>44.8±4.9</td>
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<td>Duration of menstruation (d)</td>
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<td>10.0±4.9</td>
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<tr>
<td>Number of patients with clots</td>
<td>67 (82)</td>
<td>68 (87)</td>
<td>86</td>
<td>100</td>
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<tr>
<td>Duration of clots (d)</td>
<td>3.1 (2.7)</td>
<td>3.5 (2.7)</td>
<td>2.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Pictorial chart</td>
<td>810 (300–4,000)</td>
<td>792 (200–2,100)</td>
<td>683 (400–953)</td>
<td>642 (380–855)</td>
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<tr>
<td>Dysmenorrhea</td>
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<td></td>
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<tr>
<td>Moderate</td>
<td>18 (22)</td>
<td>16 (21)</td>
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<td>Severe</td>
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<td>15 (19)</td>
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<td>14</td>
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<td>Uterus</td>
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<tr>
<td>Avetverted</td>
<td>64 (78)</td>
<td>66 (85)</td>
<td>5 (83)</td>
<td>5 (71)</td>
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<td>Midposition</td>
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<tr>
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<td>9 (12)</td>
<td>1 (17)</td>
<td>2 (29)</td>
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<td>1 (14)</td>
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<td>Hemoglobin (mmol/L)</td>
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<td>FSH (international units/L)</td>
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<td>12.4 (15.5)</td>
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<td>Uterine length (cm)</td>
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<td>Endometrial thickness (mm)</td>
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</tr>
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</table>

FSH, follicle-stimulating hormone. Data are mean±standard deviation, n (%), %, or median (minimum–maximum).

**Fig. 2.** Patient satisfaction at 4 weeks, 6 months, and 12 months. Repeated-measure analysis indicates that both the treatment effect and the effect in time on patient satisfaction are statistically significant (P < .001).

therm group (relative risk 0.29, 95% CI 0.12–0.67). Furthermore, a total of four patients underwent a hysterectomy in the bipolar group compared with eight in the hydrotherm group (relative risk 0.49, 95% CI 0.15–1.5).

**DISCUSSION**

In this randomized clinical trial, we studied two second-generation endometrial ablation techniques during the first year after treatment. The bipolar radiofrequency endometrial ablation device performed better than hydrothermablation in terms of patient satisfaction, amenorrhea, and menstual bleeding as scored on the mean pictorial chart score. We analyzed the study according to intention to treat. Three women in the hydrotherm group received the bipolar radiofrequency procedure because of a technical defect of the hydrothermablation device. The most reinterventions were performed after 6 months. We expect that these reinterventions can influence the results of both groups, but especially the outcome of the hydrotherm group. The amenorrhea rate of the hydrotherm group is higher than expected probably as a result of the fact that 35% had a reintervention of which nine hysterectomies were performed. These women were scored as amenorrheal and were satisfied with the result of the reintervention.

We choose to consider women who had a hysterectomy as amenorrheal. By doing so, we basically evaluated the effect of two strategies, of which hysterectomy was a part. Alternatively, one could consider patients who had additional hysterectomy as failures. However, in that case, one has to make assumptions on the pictorial chart scores, because these women were amenorrheal after their hysterectomy.

As shown in Table 1, the average hemoglobin was approximately 8.1 mmol/L in both groups. Women in The Netherlands are seen by their general practitioner first. When they visited the hospital, they were already treated with iron therapy if there was anemia. These women would not show a low hemoglobin or hematocrit level. That is why we did not select the patients with anemia but used the pictorial chart score to select patients.

The operation time for the bipolar endometrial ablation was less than half that of the hydrotherm
procedure. This shortens operating room time and may be an important advantage in an outpatient setting. We have not performed an analysis of cost-effectiveness. Hydrothermablation is feasible and acceptable in the outpatient setting, but the ablation cycle takes approximately 10 minutes compared with 90 seconds with the bipolar radiofrequency procedure. The very short ablation procedure of the bipolar radiofrequency device, however, makes it a promising ablation technique for outpatient treatment.

The amenorrhea rate of the bipolar group was comparable with previously reported studies (41–58%). We expected the hydrotherm group to do better, especially in women with small intracavitary pathology, because the circulating hot water has the possibility to contact the entire endometrial surface regardless of the shape of the uterine cavity. By including women with small intracavitary abnormalities, we suspected the bipolar radiofrequency device to be less successful. However, we found a lower amenorrhea rate in the hydrotherm group compared with the bipolar group, but also lower than reported in previous studies using hydrothermablation and comparing the hydrothermablation with rollerball endometrial ablation (40–44%).

In most reported studies, hydrothermablation is performed after gonadotropin-releasing hormone pretreatment. This treatment thins the endometrial layer and thus might give better treatment results. We wanted to perform an everyday practice study and decided to schedule the procedure just after menstruation.

The patient satisfaction after bipolar radiofrequency endometrial ablation is comparable to other studies (90–92%) and slightly lower in the hydrotherm group (73%). There is a high reintervention percentage compared with other studies (5%). The study of Guillot et al was a retrospective study; it could be that the hysterectomies were underreported. It is possible that gonadotropin-releasing hormone pretreatment is necessary for an optimal result in the hydrotherm group. This is a disadvantage for the hydrothermablation device in view of the costs and adverse side effects of gonadotropin-releasing hormone. In our study, only three patients (4%) in the bipolar group underwent a hysterectomy in the year after treatment; this percentage is lower than presented in previous studies (4.8–8%).

Both second-generation ablation techniques used in this study are safe and easy to perform. However, based on the results of the current randomized trial, bipolar endometrial ablation appears to offer higher patient satisfaction and amenorrhea rates.

REFERENCES


